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Major Article

Morbidity of schistosomiasis mansoni in a low endemic setting in Ouro Preto, Minas Gerais, Brazil

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Abstract

Introduction: Despite the advances of disease control programs, severe forms of schistosomiasis are prevalent. The prevalence of the disease in areas frequented by tourists urges for permanent prevention and control. The aim of this study was to describe the morbidity of schistosomiasis in the district of Antônio Pereira, Ouro Preto, Minas Gerais, Brazil. **Methods:** The proportion of positives was defined by Kato-Katz coproscopy and urinary POC-CCA rapid test. Hepatosplenic form was diagnosed using abdominal ultrasound. **Results:** Out of 180 participants,97 were examined by Kato-Katz, with 4 (4.1%) being positive. Thirty-four (22.1%) out of 154 were positive by POC-CCA. Five (2.8%) of 177 examined by ultrasound had hepatosplenic form. One of them had undergone splenectomy. One (0.6%)participant had myeloradiculopathy. **Conclusions:** Severe forms of schistosomiasis are still prevalent in low endemic areas and should be thoroughly investigated.

Keywords: Schistosomiasis mansoni. Hepatosplenic schistosomiasis. Kato-Katz. POC-CCA. Abdominal ultrasound.

INTRODUCTION

Brazil has the highest burden of schistosomiasis in the Americas. Six million people are infected and 25 million live in endemic areas[1]. The State of Minas Gerais has the largest endemic area in the country, with 523 (61%) out of 853 municipalities affected[2]. Chronic forms prevail in endemic areas. The hepatosplenic form affects 6% of infected people. It is the main cause of morbidity caused by schistosomiasis and is characterized by spleen enlargement, portal hypertension, esophageal varices, and recurrent hematemesis[3]. Abdominal ultrasound (US) is the standard method for the diagnosis of liver fibrosis caused by schistosomiasis, owing to its high sensitivity and specificity. To minimize the intrinsic variability of the investigation method, the examination follows a specially designed protocol[3-5].

Kato-Katz parasitological method is widely used to diagnose schistosomiasis infection[6]. However, it has limited sensitivity due to daily variability of eggs shedding in feces in low prevalence areas[7], which require highly sensitive methods for disease diagnosis and control. Accuracy of the urinary test for the point of care detection of the *Schistosoma mansoni* circulating cathodic antigen (POC-CCA) has been documented in high and medium prevalence areas. The test performance in low prevalence areas is not completely understood. Test performance and reading does not require specialized training and the result is available in 20 minutes at the point of care, allowing immediate treatment of the positives[8].

The increasing demand for ecotourism in Minas Gerais have raised concerns about schistosomiasis in the state's tourist areas. Mollusk species that are intermediate hosts for *S. mansoni* were identified along the Royal Route, a tourist project of national importance[9]. Ouro Preto is in the New Route branch of the Royal Route Project, where the authors identified six species of *Biomphalaria*, three of them capable of transmitting schistosomiasis mansoni. Beyond the historic and artistic heritage sites, tourists also visit the natural attractions in and around Ouro Preto. This is an additional reason to investigate and control schistosomiasis endemic to the area.

The primary objective of the study was to describe the frequency of the hepatosplenic form among the adult population in Antônio Pereira, a District of Ouro Preto-MG, using abdominal ultrasound examination. The secondary objective was to estimate the percentage of positivity in the area by the standard Kato-Katz method and by the urinary POC-CCA test.

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METHODS

Study design: this was a transversal study of the morbidity of schistosomiasis in Antônio Pereira, District of Ouro Preto, Minas Gerais, Brazil. The district is 26km North of the City of Ouro Preto-MG, accessed by fully paved road. We visited the locality to collect data between June 2012 and April 2013. Data were recorded in a structured form by interview and physical and abdominal ultrasound examination. Blood and urine samples were also collected. Each participant received a plastic container for feces and was requested to deliver the sample to the local health unit to be collected by the research team within the next two days. All participants received a printed invitation letter containing details on data collection and were personally instructed by the local health care team to attend the data collection at the pre-arranged date at 7am, after an 8h fast.

Sample size: the study population comprised the residents of Antônio Pereira, a total of 5,959 people registered in the Primary Care Information System (SIAB). The software Epi-Info, version 6.0 (CDC, Atlanta, USA), was used for sample size calculation. Parameters considered were: average schistosomiasis prevalence previously reported by the National Schistosomiasis Control Program (PCE), 17.3% in 2003 and 6% in 2010 (data informed by the Epidemiologic Surveillance authority of Ouro Preto), confidence limits of 2.5%, power of 80%, plus 20% losses. A sample size of 360 participants was calculated. After district mapping, a systematic balanced sample of 360 subjects was built inviting one person from one of every 4 houses in each street, thus covering the full extent of the district. Inclusion criteria were residency in the district for at least 5 years, age greater than 16, and written consent. Those between ages 16 and 18 had a legally responsible adult as cosignatory. Exclusion criteria were residency in the district for less than 5 years, age younger than 16, non-provision or withdrawal of consent after signing.

Data collection: mapping was accomplished by recording the longitude (x) and latitude (y) coordinates for each building using Global Positioning System (GPS) equipment, and creating thematic maps of the distribution of events in the Geographic Information System (GIS). Clinical and epidemiological information was recorded in the structured interview form: demographic, socioeconomic, behavioral, exposure to hepatitis virus (tattoo, piercing, surgery, dental procedure, and manicures), history of schistosomiasis, signs and symptoms, vital signs, anthropometry, general and abdominal physical examination.

All US examinations were performed by the same examiner, trained in the execution of the Niamey-Belo Horizonte protocol[5]. He used a portable ultrasound system GE Logic i (GE Healthcare, Chalfont St. Giles, UK) with a polyfrequency convex transducer of 2.5 to 5MHz. Portal, splenic and mesenteric veins caliber, left and right liver lobes and spleen longitudinal diameter, gallbladder wall thickness, liver fibrosis pattern, the presence of collateral circulation and abdominal lymph nodes were all recorded in the same structured form. Other abdominal or hepatobiliary findings were also recorded.

All parasitological examinations were performed in the research laboratory by the Kato-Katz method[6]. Samples were provided by the participants, stored in a fridge and processed by the research team within 2 days. Two slides were prepared for each sample with the standard weight of 41.7mg.Samples were examined by optical microscopy after 30 minutes cleansing. Samples with viable eggs of *S. mansoni* were considered positive. The number of eggs observed was recorded and multiplied by the correction factor 24 to obtain the number of eggs per gram of sample (EPG). Infection was graded as light (1-99 EPG), moderate (100-399 EPG) or intense (≥ 400 EPG). For each sample, the slide with the higher egg count was considered for the analysis. The presence of eggs of other parasites was recorded. Ten percent of all samples were re-examined by a senior technician for quality control. A third reading was undertaken to clear any doubts or disagreement.

Circulating cathodic antigen (CCA) of *S. mansoni* was searched in fresh urine samples with the POC-CCA test [For qualitative detection of Bilharzia (Schistosoma), Rapid Diagnosis, Pretoria, South Africa, batch number: 33107], following package insert instructions. The test kits were directly imported from the manufacturer in Pretoria, South Africa, and were available on site. One midstream urine sample was provided by each participant and analyzed immediately. One drop of fresh urine followed by one drop of buffer solution was deposited in the well. The test result was read in 20 minutes. Tests were considered valid if a red line appeared in the control region of the cassette. Valid tests were considered positive if a red line also appeared in the test region of the cassette. Trace lines were considered positive.

Venous blood sampling adhered to universal biosafety practices. Samples were immediately sent for laboratory processing. Hematology, coagulation and biochemistry tests were performed. Samples for analyzing the hematologic parameters were collected in tubes containing ethylenediaminetetraacetic acid (EDTA) and processed in a semiautomatic counter (ABX Micros 60 Horiba, Japan), by the impedance method for cell count and hematocrit, and photometry for hemoglobin concentration. Global and differential white cells, erythrocytes, hematocrit, hemoglobin concentration, hematimetric and platelet number per milliliter were recorded. Samples for coagulation tests were collected in tubes containing citrate and analyzed by photometry method for clot detection (Humaclot Junior Human, Germany). Prothrombin time (PT) and partial activated thromboplastin time (APTT) were obtained by the clot forming method. International Normalized Ratio (INR) was obtained by the ratio between patient PT and the average PT of the reference standard. Biochemistry analysis were performed by spectrophotometry in serum samples from anticoagulant-free tubes (CM200 Wiener, Argentina). Creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gammaglutamyltransferase (GGT) and albumin concentrations were obtained (colorimetric kinetics for creatinine, modified Szasz method for GGT, kinetic UV for AST and ALT, and bromocresol green for albumin, Bioclin, Brazil).

Statistical analysis: print data sheets were digitalized using Teleform, Version 10 (Cardiff, Wales, UK). Statistical Package for Social Sciences(SPSS) Version 18 (IBM Company,

Chicago, IL, USA) was used for statistical analysis. Quantitative data were described by central and dispersion measures. Qualitative data were described by the proportions. Agreement between tests was analyzed by the *kappa* statistics[10] with 95% exact confidence interval (95% CI). Statistical significance level was established at 5%.

Ethical considerations

This study was approved by the Ethics Board of the *Universidade Federal de Ouro Preto*. It agrees with the Helsinki Declaration of 1964, as revised in 1975, 1983, 1989, 1996, and 2000. All participants with positive parasitological tests received specific anti-parasitic therapy. Those with chronic forms of schistosomiasis or other pathologies were referred to specialized care.

RESULTS

Of 360 people invited, 180 (50%) participated in the study. Demographic, epidemiological, clinical and laboratory characteristics of the 180 study participants are shown in **Table 1**.

No participant presented jaundice, ascites or abdominal collateral circulation on physical examination. One person had a palpable liver 11cm below the costal margin at the midclavicular line and xiphoid appendix. Two (1.3%) men had paraparesis or paraplegia. One of them, a man of 37, had myeloradiculopathy (MR) caused by schistosomiasis. Platelet counts, liver enzymes, International Normalization Ratio (INR), albumin, and serum creatinine results are also presented. Platelet counts below 143,000cells/mm^3 were detected in 16 (9%) participants in the present study. Two of the five participants with hepatosplenic schistosomiasis were correctly identified by the low platelet count (*kappa* 0.135; CI 95% 0.014-0.255). One individual with a platelet count of 75,000 had evidence of hepatosplenic disease on ultrasound and another one, with 130,000 had undergone splenectomy because of decompensated hepatosplenic schistosomiasis. All the others with low platelet counts had normal US examination.

Ninety-seven (53.9%) participants provided samples for the parasitological test and 4 (4.1%) were positive with *S. mansoni* eggs. Recorded egg counts were 552 EPG in one sample, 72 EPG in another, and 48 EPG in two. Urine samples were obtained from 154 participants, and 34 (22.1%) were positive. Eighty-one (45%) participants had both tests. Agreement between POC-CCA and Kato-Katz is presented in **Table 2.** It was considered fair by the calculated *kappa* statistic of 0.216 (p-value 0.002; 95% CI 0.081-0.351).

Information on abdominal US of 177 participants is shown in **Table 3**. Five (2.8%) of them, with ages between 30 and 60, had hepatosplenic schistosomiasis, characterized by liver and spleen enlargement and periportal fibrosis. One 30-year-old man with hepatosplenic form had undergone splenectomy due to variceal bleeding secondary to portal hypertension. None of the participants presented marked liver border irregularities, abdominal lymph nodes or collateral vein circulation on US. One woman and 4 men had pattern D of fibrosis[5]. Cholelithiasis was diagnosed in 7 (4%) participants and liver steatosis in

TABLE 1: Demographic, epidemiological, clinical and laboratory characteristics of 180 study participants in Antônio Pereira, Ouro Preto, Minas Gerais, 2012-2013.

Characteristic	Number	Percentage
Women	93	51.7
Schooling		
Illiterate	9	5.0
Primary school	59	33.0
Secondary school	64	36.0
Higher education	7	4.0
Previous treatment for schistosomiasis	19	10.6
Gastrointestinal bleeding	14	7.8
Blood transfusion	9	5.0
Tattoo or piercing	20	11.1
Alcohol drinking	61	33.9
Dental procedure	125	69.4
Surgery	71	39.4
Manicure	69	38.3
Systemic arterial hypertension	42	23.3
Positive rapid test for hepatitis B	3	1.7
Palpable liver	25	13.9
Palpable spleen	4	2.2
	mean	**standard deviation**
Age (years)	39.9	16.5
Weight (kg)	68.8	14.0
BMI = weight (kg)/(height (m))^2	25.5	5.0
Platelet count (10^3/µL)	204,079	56,980
ALT (UI/L)	20.97	14.38
Albumin (g/dL)	4.33	0.26
INR	1.01	0.03
Creatinine (mg/dL)	0.86	0.17

BMI:body mass index; **ALT(UI/L)**: alanine aminotransferase (international units per liter); **INR**:International Normalized Ratio.

TABLE 2: Agreement between Kato-Katz and POC-CCA* tests in Antônio Pereira, Ouro Preto, Minas Gerais,2012-2013.

	Kato-Katz		
POC-CCA	**positive**	**negative**	**Total**
Positive	2	12	14
Negative	0	67	67
Total	**2**	**79**	**81**

kappa: 0.216; 95% Confidence Interval: 0.081-0.351; p-value: 0.002. **POC-CCA:** Point of Care Circulating Cathodic Antigen.

22 (12.4%). Six (3.3%) had abdominal scars compatible with cholecystectomy and the gallbladder could not be identified on US.

Agreement between physical examination and abdominal ultrasound, and parasitological and urinary tests are presented in **Table 4**. Kato-Katz (KK) had fair agreement with palpable spleen and increased spleen diameter on US. POC-CCA had poor agreement with portal hypertension.

DISCUSSION

The main indicator used by the National Program of Surveillance and Control of Schistosomiasis (PCE) in parasitological surveys is the positivity percentage, considered a proxy to the prevalence. The 4.1% found in the study area is similar to the national average of 4.5%, described in 2012[1]. PCE acts by detecting positive cases in regular parasitological surveys, for treatment of the positives with praziquantel. In one analysis of the impacts of the program, Amaral et al[11] described a 38.5% reduction of the percentage of positives since the beginning of the program in 1976 until the analysis in 2003. In Minas Gerais, the average positivity found between 2004 and 2007 was 5.3%, with reductions also demonstrated at the municipality level[2]. In Ouro Preto, PCE registered a consistent reduction of positivity from 17.3% in 2003 to 6% in 2010 (data informed by the Epidemiologic Surveillance authority in Ouro Preto) as detected in the present study. As no further survey had been accomplished in the locality since 2010, the results of the present study were immediately reported to the local surveillance authorities.

According to the present survey, the area has results lower than the target of 5% positivity established for surveillance and control. However, the population in this study was older than 16, as opposed to the priorities established for testing by the PCE. The program targets school age children of 6-15, as they might present the highest positivity rates and parasite burden and reflect the real prevalence in the community[1]. Positivity found here might have been underestimated by the low sensitivity of the Kato-Katz method due to egg shedding variability[7], or to the progressively reduced egg counts after successive treatments with praziquantel[2].

In this context, it is desirable to investigate alternative diagnostic tests for the detection of schistosomiasis with the improvement of disease control. POC-CCA has been

TABLE 3: Abdominal ultrasound of 177 participants in the study in Antônio Pereira, Ouro Preto, Minas Gerais, 2012-2013.

Length (cm)		**Mean**	**Standard deviation**
Left liver lobe		8.7	1.8
Right liver lobe		12.8	2.3
Spleen		9.5	1.3
Portal vein caliber		1.0	0.2
Splenic vein caliber		0.67	0.2
Superior mesenteric vein caliber		0.76	0.2
Gallbladder wall thickness		0.19	0.12
		Number	**%**
Fibrosis pattern*	A	117	66.1
	B	55	31.1
	D	5	2.8

*Patterns of liver fibrosis as described in the Niamey-Belo Horizonte protocol for ultrasound evaluation in schistosomiasis [5]

TABLE 4: Comparison of clinical and ultrasound findings with Kato Katz and POC-CCA* results, in Antônio Pereira, Ouro Preto, Minas Gerais, 2012-2013.

	Kato Katz				POC-CCA			
Clinical findings	**negative(%)**	**positive(%)**	***kappa* (IC 95%)**	**p-value**	**negative(%)**	**positive(%)**	***kappa* (IC 95%)**	**p-value**
Non-palpable spleen	90(96.8)	3(3.2)	0.314(0.125-0.503)	**0.001**	110(76.9)	33(23.1)	0.004(-0.086 -0.094)	0.928
Palpable spleen	1(50.0)	1(50.0)			3(75.0)	1(25.0)		
Non-palpable liver	75(94.9)	4(5.1)	-0,072(-0.226-0.082)	0.358	94(74.6)	32(25.4)	-0.126(-0.281-0.029)	0.110
Palpable liver	16(100.0)	0(0.0)			19(90.5)	2(9.5)		
Ultrasound								
Liver fibrosis absent	68(95.8)	3(4.2)	-0,001(-0.129-0.128)	0.990	77(75.5)	25(24.5)	-0.073(-0.231-0.085)	0.367
Liver fibrosis present	23(95.8)	1(4.2)			37(82.2)	8(17.8)		
Portal hypertension absent	69(95.8)	3(4.2)	0,003(-0.129-0.134)	0.970	92(82.1)	20(17.9)	0.197(0.0352-0.358)	**0.017**
Portal hypertension present	22(95.7)	1(4.3)			22(62.9)	13(37.1)		
Normal right liver lobe	84(95.5)	4(4.5)	0.059(-0.246-0.128)	0.538	106(76.3)	33(23.7)	-0.055(-0.178-0.069)	0.383
Small right liver lobe	8(100.0)	0(0.0)			8(88.9)	1(11.1)		
Normal left liver lobe	47(97.9)	1(2.1)	0.041(-0.039-0.122)	0.305	55(73.3)	20(26.7)	0.074(-0.212-0.0611)	0.278
Increased left liver lobe	45(93.8)	3(6.3)			59(80.8)	14(19.2)		
Normal spleen diameter	90(96.8)	3(3.2)	0.259(0.061-0.457)	**0.010**	111(78.2)	31(21.8)	0.049(-0.051-0.150)	0.339
Increased spleen diameter	2(66.7)	1(33.3)			3(60.0)	2(40.0)		

POC-CCA: Point of Care Circulating Cathodic Antigen.

found similar to Kato-Katz in areas of high prevalence, but its performance in low prevalence areas still needs further studies[12]. In the present study, we performed POC-CCA in parallel to the parasitological method. The positivity for the urinary test was more than five times higher than Kato-Katz. This could be explained by the reduced sensitivity of the parasitological method performed in one single sample[7], by the lower specificity of the urinary test in low transmission areas[13], or because of the counting of trace results as positives[14]. The analysis of accuracy of the urinary test was not possible in this study because of the reduced number of participants.

Kato-Katz is usually regarded as unsatisfactory as a reference method, especially in low prevalence areas. In the present work, 2 slides of one stool sample were prepared for microscopic analysis, as currently recommended by the Brazilian Ministry of Health for schistosomiasis control. Siqueira et al[15] compared Kato-Katz and a molecular method for the diagnosis of schistosomiasis in a low transmission area. The authors performed Kato-Katz with 12 slides per sample as compared to 2 slides per sample. The positivity rates found were 14.4% and 8% respectively. Their results further emphasize the low sensitivity of the stool microscopy, and the need to improve accuracy in defining the prevalence in low transmission areas for an effective control of the disease.

Trace results in the POC-CCA test were considered positive in the present study. According to the test kit package insert, the intensity of the line is qualitatively related to the intensity of the infection, but no specific instructions were provided by the manufacturer on the interpretation of trace lines. No semi quantitative analysis was performed in the present report. The subject of trace line readings remains a matter of debate. One prospective study examined school-age children in a high endemic area of Uganda and compared POC-CCA with Kato-Katz at baseline and after multiple treatments with praziquantel[16]. The authors used six Kato-Katz stool samples as gold-standard to analyze POC-CCA performance with trace result considered as either positive (t+) or negative (t-). Prevalence with t+ was 88.2% as compared to 78.9% with t-. POC-CCAt+ showed moderate agreement with the gold-standard (*kappa*: 0.42) only at baseline, but POC-CCAt- agreement improved from fair to moderate one month after first treatment. These results did not allow conclusions about the best interpretation of trace results, especially in low endemic areas.

Trace readings were also considered positive as per manufacturer's instructions in another study that assessed day-to-day variability of POC-CCA readings by performing tests on consecutive days[17]. POC-CCA showed lower variability on three consecutive days when compared to three consecutive days of Kato-Katz (18% and 48%, respectively). However, the authors notice that most variation occurred in the lower intensity end of POC-CCA reading spectrum, involving the trace reading records. Their results add further complexity to the interpretation of trace results.

In attempting to improve accuracy and to provide a better understanding of the interpretation of trace results of POC-CCA in low prevalence areas, Coelho et al[14] proposed a 10-fold concentration of urine samples through lyophilization as a further step to the execution of POC-CCA. The authors compared POC-CCA with a gold-standard defined as the combined results of 24-smear Kato-Katz and Saline Gradient, a total of 1g of feces analyzed per individual. In their study, a prevalence of 2% detected in non-concentrated urine sample increased to 32% when lyophilized urine was used, compared to 30% found with the gold-standard. Sensitivity of POC-CCA increased from unacceptable 6% to 56% after lyophilization. Nearly 50% of all negative urine samples were defined as positive after concentration when compared to 24-smears Kato-Katz, and almost one third became positive after concentration when compared to 2-smears Kato-Katz. Interpretation of trace results was also influenced by urine concentration. POC-CCA results with non-concentrated urine had poor agreement with parasitological tests, whereas moderate agreement (*kappa* 0.401) was found after urine concentration, but only when trace results were considered negative. This finding suggests that interpreting trace results as positive might lead to the misuse of praziquantel to treat healthy individuals.

Despite the advances in the interpretation of POC-CCA results, controversy remains regarding the accuracy of parasitological methods used as gold-standard. Studies of accuracy especially designed and using appropriate Bayesian statistical methods to overcome the absence of a true gold-standard method are required to help understand the utility of POC-CCA in low endemic areas[17,18].

Blood tests were performed to screen for additional health conditions and to help to define morbidity by schistosomiasis. Albumin, INR and ALT serum levels were determined to screen for confounding liver diseases. All participants tested within the normal range. Platelet counts below 143,000cell/mm^3 were shown to predict hepatosplenic schistosomiasis in an endemic area with a prevalence of 23%[19]. However, the accuracy of low platelet count to identify hepatosplenic schistosomiasis in lower prevalence areas is unknown.

There is no consensus about the prevalence of renal disease in schistosomiasis mansoni. A recent report described a 12.7% prevalence of glomerulonephritis in patients with hepatosplenic schistosomiasis[20]. The low prevalence of hepatosplenic form (2.8%) may explain why all participants had normal creatinine levels. All patients with this advanced form were referred to specialized care for in-depth investigation of renal function.

Despite the low positivity in parasitological tests, severe forms of the disease were found in Antônio Pereira: 2.8% of all participants presented the hepatosplenic form and one had myeloradiculopathy. It may reflect a selection bias, as people affected by diseases are usually more prone to participate in studies of interest. Drummond et al[21] have previously described morbidity data on schistosomiasis in Minas Gerais, obtained at a specialized health care unit after intensive surveillance between 2002 and 2005. During the period, 129 patients were identified, 75 (58.1%) with the hepatosplenic form and 54 (41.9%) with MR. The authors believe that morbidity of schistosomiasis remains underestimated and strongly recommend surveillance to identify cases in areas of low prevalence and they recommend surveillance of the myeloradiculopathy form where early diagnosis and treatment can prevent permanent incapacity.

The present study offers an unprecedented description of the morbidity of schistosomiasis in Ouro Preto, MG. In contrast with

the urban area which is visited mainly because of the historic and artistic interest, the study area and the surroundings are visited mainly because of the natural attractions. This can result in risk of contamination of visitors and spread of the disease to other areas. The present study adds information about the local endemic and the needs for control, prevention and health care actions towards the population and study area.

The main limitations of this study are related to the low adherence to parasitological survey, and the analysis of only one sample per participant. Despite the efforts to mobilize the community through local radio announcement and active participation of the local Primary Health Care team, there was a 50% loss from the calculated sample size, and only slightly more than half of the participants provided a feces sample. This fact reinforces the need for the development of less laborious diagnostic tests, such as the POC-CCA. The analysis of only one feces sample per person may have underestimated the prevalence of schistosomiasis and undermined the evaluation of the alternative urinary test. But this option was taken to reproduce the PCE protocol, and thus resemble its actual performance.

In conclusion, this study detected severe forms of schistosomiasis including hepatosplenic form and MR in the low endemic setting in Ouro Preto-MG. These findings reinforce the need for permanent surveillance of the severe forms of schistosomiasis in low endemic areas despite the advances of the control program in Brazil. In addition, studies especially designed to evaluate alternative diagnostic methods are required to cope with the advances of infection control in endemic areas.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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