



Impact of Mass Praziquantel Administration for Controlling *Schistosoma haematobium* Infection in Schoolchildren from Bamako, Mali

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Authors' contributions

Author AD participated in the conception and design of the study, data analysis, and interpretation. He also contributed to the writing of the paper, and assured the coordination of the trial. He has reviewed the final version. Authors MD and AZD participated in the design of the study and onsite execution by collecting and analyzing the data. They also contributed to the writing of the paper. Authors SS and ST participated in the conception and onsite execution, and assisted in praziquantel distribution and the assessment of side effects. Author OD participated in the conception and design of the paper. He contributed to the data analysis, the writing of the paper, and reviewed the final version. All authors read and approved the final paper.

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ABSTRACT

Background: Uro-genital schistosomiasis caused by *Schistosoma haematobium* is prevalent in sub-Saharan Africa. For the control of the disease, the frequent and periodic use of mass praziquantel administration (MPA) is recommended. However, despite of several preventive chemotherapy campaigns implemented in Mali since 2005, schistosomiasis rests endemic in the district of Bamako. This study aimed to assess the impact of MPA on *S. haematobium* prevalence

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and intensity in schoolchildren from Bamako between 2011 and 2014.

Materials and Methods: From February to March 2014, a cross-sectional survey has been conducted in twenty-nine schools throughout the six municipalities (MI-VI) of Bamako. Urine samples (10 mL) were collected from 10 h to 14 h p.m. and examined for *S. haematobium* ova using the filtration technique.

Results: Of the 672 schoolchildren aged 8 to 15 years old, 349 (51.9%) were males and 323 (48.1%) were females. The prevalence of the infection was 16.2% (109/672) (CI95%; 16,1-16,3). The geometric mean egg count (GMEC) was 0.1639. Notwithstanding MPA strategy implementation, the infection rates were comparable ($p=0.46$), despite of the globally increase of infection ranged from 14.7% in 2011 to 16.2% in 2014. At the same period, now the prevalence significantly decreased in M-II ($p=0.018$), now it increased in M-V ($p=0.0039$). The intensity of infection was uniform across the age groups, sex, the various municipalities and the Niger River banks ($p>0.05$).

Conclusion: Our findings show a mitigated overcome of the MPA strategy on *S. haematobium* prevalence in the urban area of Bamako. So, persistent prevalence of infection suggest that besides periodic drug distribution, introduction of proper sanitation is imperative among the communities especially around the Niger River banks and its tributaries in order to curtail the transmission and morbidity caused by schistosomiasis in this area.

Keywords: *Schistosoma haematobium*; mass praziquantel administration; prevalence; intensity; Bamako; Mali.

1. INTRODUCTION

Schistosomiasis is an ancient disease of poverty caused by blood Trematoda of the genus *Schistosoma* [1-3]. Transmission is closely linked with human practices related to water contact and sanitation. Hence, schistosomiasis mainly affects people who live in poor or marginalized communities in the tropics and subtropics. According to the Global Burden of Disease Study 2010 (GBD 2010), schistosomiasis ranks third after leishmaniasis and soil transmitted helminthiasis among the neglected tropical diseases (NTD) and is responsible for an estimated 3.3 million disability-adjusted life years (DALYs) [4]. In 2012, the World Health Organization (WHO) announced the new goals for 2020, namely to eliminate several of the NTD and to intensify control of other NTD, so that they no longer pose public-health problems [5]. Specifically, the aim for schistosomiasis-endemic countries is to periodically administer the antischistosomal drug praziquantel to populations at risk of infection (school-age children, women, fishermen, farmers.) and hence prevent morbidity. This strategy called "preventive chemotherapy" (PC) is aimed at optimizing the large-scale use of safe, single-dose medicines and offers the best means of reducing the extensive morbidity associated with four helminthiasis (lymphatic filariasis, onchocerciasis, schistosomiasis and soil-transmitted helminthiasis) [6]. The primary goal, as endorsed by member states in World Health Assembly (WHA) resolution 54.19 in 2001 is to

treat at least 75% of school-aged children (SAC) who are at highest risk of morbidity [7,8]. Even if the schistosomiasis control strategy announced in 2001 (WHA54.19), then currently notified in the 2006 guidelines targeted to prevent morbidity, some countries intensified control efforts to significantly reduce transmission (Burkina Faso, Cambodia, China, Egypt, Morocco and Mauricio) [9-11]. So, the sixty-five Session of WHO (WHA65.21) [12] henceforth, took into consideration schistosomiasis elimination announced in WHA54.19 resolution, feasible in some epidemiological areas due to a strong political engagement to reach the objective [13,14]. However, whatever all these endeavor, schistosomiasis is far to be controlled in many parts of tropical and subtropical countries. In cause, the primary goal WHA54.19 resolution adopted in 2001 has not been achieved. So, in 2010, only 12.2% of people at risk for morbidity due schistosomiasis and 22.8% of SAC at risk for morbidity due to STHs received PC for praziquantel and Benzimidazoles.

In Mali, the mass praziquantel administration (MPA) has been implemented since 2005 to reach the WHA54.19 targeted goal. To attain this goal, the eligible population of SAC was submitted to a yearly or biannual PC campaign in schistosomiasis-endemic areas. In the district of Bamako where the prevalence of *Schistosoma haematobium* was 14.7% in 2011 [15], the MPA strategy has been used according to the Schistosomiasis National Control Program recommendations. The study aimed to appraise

the impact of MPA campaigns carried out since 2011 on *S. haematobium* infection in primary schoolchildren, the main carriers and spreaders of schistosomiasis. We hypothesized that MPA strategy implementation should significantly reduce prevalence and intensity of uro-genital schistosomiasis caused by *S. haematobium* in the district of Bamako.

2. MATERIALS AND METHODS

The study was conducted in Bamako (12°39' N latitude and 8°0' W longitude), the capital city of Mali. The surface area of the city is 1420 km². The town looks like a big basin, surrounded in part by hills, with the Niger River and its tributaries flowing across. The town belongs to the North-Soudanian climatic zone with two major seasons: the wet season from May-June to October with its beginning and end marked by torrential rains and thunderstorms, and the dry season from November to April-May. The mean annual rainfall is about 1,400 mm, which occurs mainly during the period from July to September. Temperatures are generally high and almost uniform throughout the year with a mean annual maximum temperature of 33°C and a mean annual minimum temperature of 22°C [16]. The tributaries of the Niger River instead of to be used to collect water from the rain, they have been turned into a refuse dump, which leads to a slow flow or stagnant water, and in turn makes them suitable breeding sites of snail intermediate hosts. In 2012, the population was 2,309,106 inhabitants, with an annual growth of 4.8% [17]. Unfortunately, this rapid and disordered growth has not been followed by improved sanitation, sewage systems, and the right water supplies. The city is partitioned into six municipalities, ranging from M-I to M-VI and more than 50 quarters (Fig. 1). There are four municipalities (I–IV) on the left bank of Niger River and two (V–VI) on the right bank. There are about 736,183 inhabitants on the left bank compared to 849,727 on the right. People first occupied the left bank, and progressively, in accordance with the city's growth due to various factors including migration, other quarters appeared around the Niger River and its tributaries. The down-town includes the municipalities M-II, M-III and one part of M-IV (ACI 2000) with most of administrative offices, the main trades mixed with the founder quarters with high population density. Many quarters of the others municipalities are peripheral with poor living conditions. Minority of the houses along Niger River are made of mud/wooden walls and tin roofs with open eaves whereas the majorities

are made of cement. The pollutants from human and animal fecal waste, water from domestic use and industrial waste flow into nearby water collection drains and depressions. Crops such as maize, gombos and vegetables are grown in small gardens close to the river and in new suburbanized areas. Domestic animals include cattle, pigs, goats, sheep, chicken, cats, dogs, rabbits, turkeys and geese co-habit with populations.

According to the seasonal characteristics of the climate in the Sahel, the infection due to schistosomiasis occurs mainly during the rainy season and lasts till water collections drying in January or February. However, transmission is permanent around the big dams of Sélingué and Manantali on Niger and Senegal Rivers respectively, and the small dams of Bandiagara in the centre of the country.

2.1 Study Design and Sample Size Calculation

The survey was conducted in thirty (30) blocks, each 200 m x 200 m, in Bamako. These blocks were selected on the basis of the images from the SPOT-5 (Satellite Pour l'Observation de la Terre), part of the National Aeronautics and Space Administration's (NASA) Earth Observing System [18], at 2.5 m of spatial resolution obtained on March 2, 2009. One school inside or nearest to each of the 30 blocks was chosen for parasitological investigations in order to study the distribution of schistosomes in Bamako. To determine the sample size, we stratified the area into two levels according to the distance from schools to the potential snails breeding sites (Niger River and/or tributaries). The schools inside the strata I, were less far 100 meters from the breeding sites. The schools inside the strata II were more than 500 meters far from the breeding sites. Inside of each of these strata, 330 schoolchildren (that means 660 at least) were selected using a simple random sampling (SRS) technique after obtaining the lists of students from school registration books. The sample size was estimated using a single proportion sample size formula by considering the following parameters: *S. haematobium* prevalence of 20%, 95% confident level, and 6% of precision.

From 2011 to 2014, praziquantel has been distributed in the district of Bamako following the scheme below:

2011: in M-II, M-V and M-VI;
2012: in M-I to M-VI;

2013: in M-II, M-V and M-VI;
 2014: any municipality received treatment

For each treatment round, the children received a single dose of praziquantel (40 mg/kg) from 15

to 20 November in 2011 and from 7 to 11 October in 2013. To evaluate the impact of treatment, the research team started parasitological survey two months after each treatment campaign.

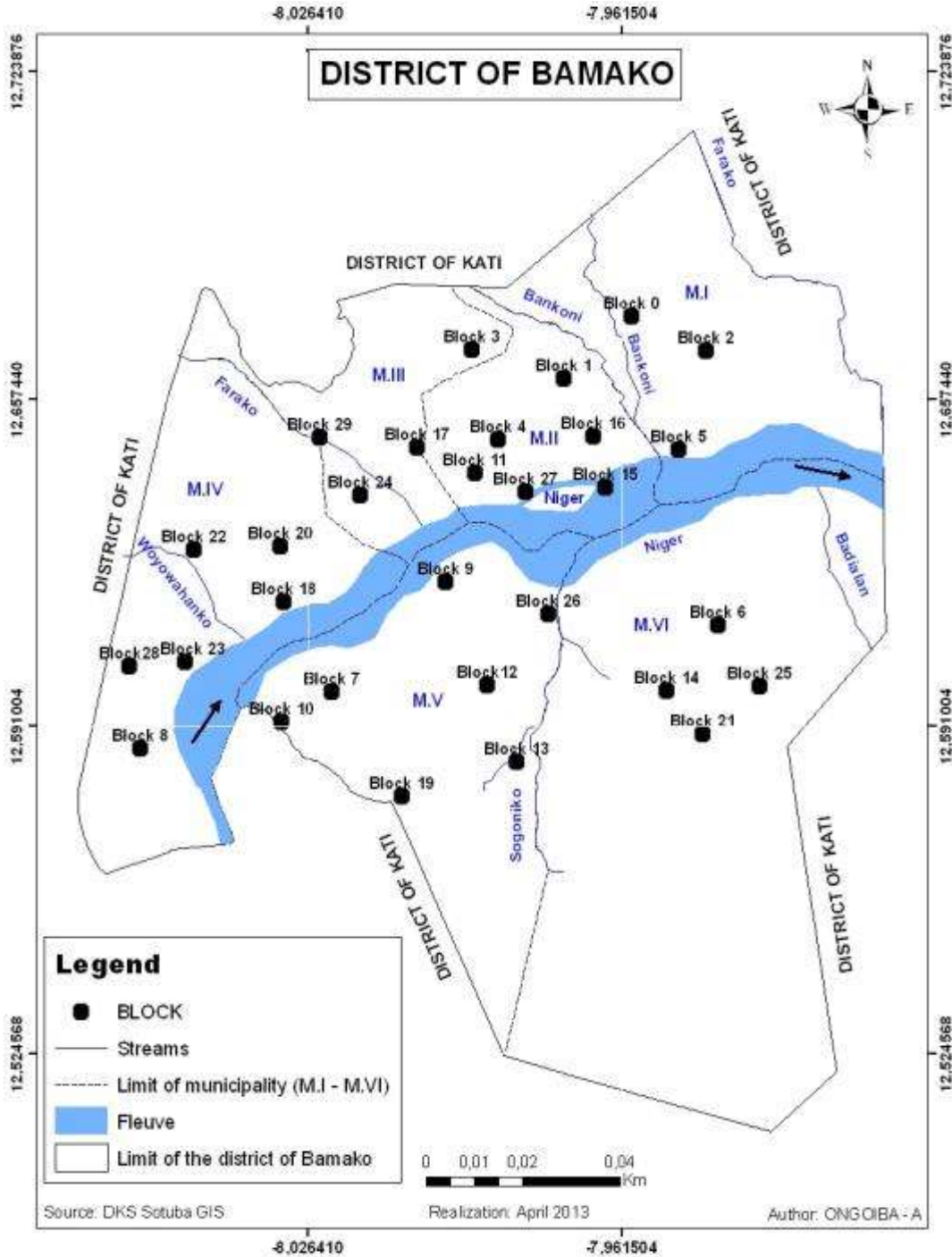


Fig. 1. Map of the district of Bamako with localization of the twenty-nine studied blocks (DEAP/MRTC, 2012)

2.2 Techniques and Data Collection Procedures

All urine samples were collected between 10 h and 14 h in the field, by trained laboratory technicians. From each subject, urine was collected in a properly labeled specimen container. Filtration technique was employed to analyze the samples. A total of 10 mL urine was taken from each specimen bottle after mixing it. The mixed sample was filtered through a nytrel filter and examined immediately under a microscope using $\times 10$ magnifications for schistosome egg characteristics [19]. The intensity of *S. haematobium* infection was expressed as number of eggs per 10 ml of urine. As a quality control measure, 10% of the filters were reexamined by a senior parasitologist for the presence of schistosome eggs.

2.3 Data Analysis

Data were double entered using Access and analyzed by SPSS (IBM, version 19) statistical software with 95% confidence intervals. The Chi-squared test was used to compare differences in prevalence. The Anova test was used to compare geometric means egg count after logarithmic transforming of *Schistosoma haematobium* egg count plus 1 ($\log_{10}(\log \text{egg count} + 1)$). A *p* value less 0.05 was considered to be significant.

2.4 Ethical Consideration

The proposal was reviewed and approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Pharmacy and Dentistry, University of Techniques and Technologies of Bamako (USTTB). Parents/guardians and school authorities provided oral consent on behalf of all participants. Only participants who provided a signed assent form were registered and requested to provide urine samples. Individuals who tested positive for schistosomiasis infection were treated with praziquantel (40mg/kg), according to the Schistosomiasis National control program guidelines. For oral informed consent obtaining, the study consent form has been translated orally into local languages and dialects in the event that a potential parents/guardians does not read or speak French. Verification that the oral translations are accurate and that the contents of the informed consent form were transmitted to the parents/guardians orally have been done by an independent witness.

Discussion of risks and possible benefits of the study have been conducted with parents and guardians. The parents/guardians have had sufficient opportunity to discuss the study and process the information in the consent form prior to agreeing to their child's participation.

3. RESULTS

Out of 672 samples examined, 109 (16.2%) were positive for *S. haematobium* (95% CI; [16.1-16.3]). The geometric mean egg count was 0.1639. Distribution of *S. haematobium* infection by age, municipalities, sex and River bank in 2011 and 2014 is shown in Table 1. According to age and sex, there was no statistically significant difference ($p > 0.05$). By contrast, with regards to the municipalities, the prevalences of infection varied significantly in municipalities II and V (Table 1). Whereas infection significantly decreased in M-II (ranged from 17.0% to 1.9%) ($p = 0.018$), it increased in M-V (ranged from 14.3% to 29.8%) in 2011 and 2014 respectively ($p = 0.0039$). With regards to the Niger River banks, while the prevalence significantly increased on the right bank ($p < 10^{-4}$), it was comparable on the left bank in 2011 and 2014 ($p = 0.05$) (Table 1).

Schistosoma haematobium geometric mean egg count (GMEC) varied from 0.1403 in 2011 (CI95%: 0.1204 – 0.1609) to 0.1639 in 2014 (CI95%: 0.1295 – 0.1982). The comparison of the two means showed any difference by the ANOVA test ($p = 0.233$).

4. DISCUSSION

The objective of our study was to assess the impact of MPA on the prevalence and intensity of uro-genital schistosomiasis caused by *Schistosoma haematobium* particularly in schoolchildren from the district of Bamako after four years preventive chemotherapy campaigns. The prevalence of 16.2% that we found in this study should be improved if two or more filters were analyzed as stated in previous studies. In Ghana for instance, the screening for three times improved the sensitivity of urine filtration by at least 22.9% as compared with single screening [20]. In two others studies, the gold standard microscopic enumeration of eggs in urine has been found to be less sensitive in low infections like our post therapeutic areas [21,22]. Compared to those of 2011 (14.7%), the mass drug administration didn't result on a significant variation in terms of the impact of the treatment

Table 1. Prevalence of *Schistosoma haematobium* among schoolchildren from Bamako by age, sex, municipalities and banks in 2011 and 2014

Study periods	2011			2014			p-value
	Positive	Total	P(%)*	Positive	Total	P(%)*	
Age (Years)							
8-10	184	1462	12.6	69	464	14.9	0.30
11-15	75	299	25.1	40	208	19.2	0.25
Total	259	1761	14.7	109	672	16.2	0.46
Municipalities							
M-I	40	179	22.3	14	113	12.4	0.10
M-II	42	247	17.0	1	53	1.9	0.018**
M-III	39	278	14.0	14	155	9.0	0.22
M-IV	82	465	17.6	42	192	21.9	0.35
M-V	46	322	14.3	36	121	29.8	0.0039**
M-VI	10	270	3.7	2	38	5.3	0.65(F)
Total	259	1761	14.7	109	672	16.2	0.46
Sex							
Male	141	902	15.6	73	349	20.9	0.07
Female	118	859	13.7	36	323	11.1	0,34
Total	259	1761	14.7	109	672	16.2	0.46
River banks							
Left	203	1169	17.4	71	513	13.8	0.05
Right	56	592	9.5	38	159	23.9	<10⁻⁴**
Total	259	1761	14.7	109	672	16.2	0.46

P(%)*: The prevalence of *Schistosoma haematobium*; **: The p value with statistical significant difference

despite of the global increase of infection passing to 16.2% in 2014. In Mali, *S. haematobium* is the most common schistosome species besides *S. mansoni*. The species is widespread in all the ecological areas (from humid Savannah to Sahel and Desert area), while *S. mansoni* is focused especially in rice irrigated zones around the dam of Sélingué and in Office du Niger [23,24] where temperatures are more convenient. The mass drug distribution adopted by the National Program for Eliminating of Tropical Diseases is focused on five diseases: trachoma, lymphatic filariasis, onchocerciasis, schistosomiasis and soil-transmitted helminths (STHs). With regards to the co-infection of populations with these pathogens, a co-administration strategy of azithromycin plus ivermectin plus praziquantel and albendazole has been adopted to treat simultaneously the listed diseases respectively in areas where both all of them are endemic. So, the endemicity of one, two or more of these diseases determined the profile of co-administrated drugs. To eliminate these NTD, the goal of the program from 2012 to 2016 is to reach every year 80% of therapeutic coverage rate of eligible populations, and 100% of geographic coverage rate of endemic areas including the district of Bamako. In contrast to the results of Bamako, in the highly-endemic region of Ségou in Mali, the authors concluded to a

significant reduction as well as in intensity and prevalence of infection on both *S. haematobium* and *S. mansoni* infections after repeated chemotherapy from 2004 to 2010 [25]. Similarly in Burkina Faso, significant reductions in the prevalence and intensity of *S. haematobium* infection were observed, one year after treatment [26]. In Upper Egypt, the impact of mass chemotherapy using praziquantel (40 mg/kg of body weight) on *Schistosoma haematobium* endemicity results to 83.6% reduction from 23.1% to 3.8%. Geometric mean egg counts decreased four-fold from 12.4 to 3.1 [27]. Usually, the impact of praziquantel results to a significant decrease of schistosomiasis infection after repeated treatment. However, in some cases due to many factors, the expected results are not achieved. Thus, after the expected yearly treatment campaign, there was an increase *S. haematobium* infection rates between 2004 and 2014 (ranged from 78.6% to 80.0%) in the sentinel sites of Diema an endemic area in the North-West of the country (Dr Dembele R, Schistosomiasis national control program, unpublished results). Both in the district of Bamako and in Diema, the irregularity of MPA campaigns in addition to the low treatment coverage reported in Diema (40%) were in cause to explain the increase of schistosomiasis prevalence. For example in Bamako, according

to the treatment scheme planned by the program, all the six municipalities were assumed to receive praziquantel in 2012; surprisingly, despite of their high infection rates, any of M-I, IV and V was covered in 2013 because of praziquantel unavailability. In our point of view, rather than treating all municipalities in the case of limited resources, it is particularly important that programme managers carry out a detailed geographical assessment of schistosomiasis in order to focus the use of praziquantel to the areas in real need. In this case, the M-IV and V established along Niger River and its tributaries, prior should received praziquantel. In some cases, the outcome of chemotherapy depends on the timing of the treatment relative to the annual transmission pattern with regards to the hypothesis based on the fact that *Schistosoma haematobium* is refractory to praziquantel (PZQ) during the prepatent period of infection. In the district of Bamako, the preventive chemotherapy is planned from October to June during school year. When the treatment took place early in December-January corresponding to the dry season, some water bodies dry up leading to a concentration of snail hosts and a high cercariae release in water. So, the praziquantel cure rate could be affected when the treatment was conducted at this period. With regard to the previous studies [27-29], it is assumed that appropriately timed praziquantel administration will enhance the impact of MPA. Following our findings, after solving the problem related to adequate period of drug administration, the schoolchildren living near water collections (Niger River and its tributaries) should be treated annually contrarily to the other to curtail transmission. In addition, in a specific urban area such as Bamako, independently to the irregularity and the timing of the drug administration, poor sanitation around water sources is a major cause of infection. To support this point, the prevalence rates of *S. haematobium* and *S. mansoni* were reduced from 45% in 2003 to zero in 2010 in the schoolchildren living along a stream called Farako in the M-IV, after it has been cleaned up by the authorities [15].

5. CONCLUSION

The implementation of MPA in Mali shows a mitigate impact on the prevalence of *Schistosoma haematobium* infection in Bamako. The study has revealed that prevalences and intensities were comparable in 2011 and 2014 despite of the global increase of the prevalence

rates observed in 2014. Such profile was not common and praziquantel mass drug administration usually results on a significant decrease of infection. While the infection increased on the right bank of Niger River Bank and in M-V, it decreased in M-II. This supports an urgent need to re-evaluate the current control measures and implement an integrated, targeted and effective schistosomiasis control measures. In support to the deworming program, introduction of proper sanitation are imperative among the communities in order to curtail the transmission and morbidity caused by schistosomiasis in this area.

ETHICAL APPROVAL

The proposal was reviewed and approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Pharmacy and Dentistry, University of Techniques and Technologies of Bamako (USTTB) (Cf. a scanned copy of the initial study). Only children whose parents and themselves accepted to participate to the study were registered and requested to provide urine samples. Individuals who tested positive for schistosomiasis infection were treated with praziquantel (40 mg/body weight), according to the Schistosomiasis National control programme guidelines.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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