

Inadequate Clearance of Circulating Cathodic Antigen Following Single-Dose Praziquantel Treatment Among Pre- and School-Aged Children in *Schistosoma mansoni* Hyper-Endemic Areas of North-Western Tanzania

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ABSTRACT

Background: Praziquantel (PZQ) remains the primary drug for treating schistosomiasis, with its efficacy traditionally measured using the Kato-Katz technique. However, these methods have limitations, prompting interest in point-of-care circulating cathodic antigen (POC-CCA) tests as an alternative diagnostic tool. This study aimed to assess the efficacy of praziquantel in clearing circulating cathodic antigen (CCA) among pre- and school-aged children in a *S. mansoni* hyper-endemic area of North-Western Tanzania.

Methods: A longitudinal study was conducted among 161 children aged 2–17 years. Participants were screened for *S. mansoni* infection using Kato-Katz and POC-CCA tests at baseline and 21 days post-treatment with a single dose of PZQ (40 mg/kg). Cure rates (CR) and egg reduction rates (ERR) were calculated.

Results: The overall prevalence of *S. mansoni* was 98 (70.0%) (Kato-Katz) and 114 (70.8%) (POC-CCA). The parasitological cure rate (PCR) was 61 (66.3%) (Kato-Katz) and 27 (27.6%) (POC-CCA), with an ERR of 73.6%. Significant differences were observed between the two diagnostic methods.

Conclusion: While PZQ demonstrated adequate efficacy based on Kato-Katz results, poor CCA clearance highlights the need for improved diagnostics and monitoring strategies in schistosomiasis control programs.

BACKGROUND

Schistosomiasis is a parasitic disease caused by blood flukes (trematodes) of the genus *Schistosoma*. There are many species of schistosomes, such as *S. haematobium*, *S. japonicum*, *S. mansoni*, *S. mekongi*, *S. intercalatum*, and *S. guineensis*, but the main species infecting human beings are *S. haematobium*, *S. japonicum*, and *S. mansoni*.¹ Schistosomiasis, caused by blood flukes of the genus *Schistosoma*, affects over 250 million people worldwide, primarily 200 million people living in sub-Saharan Africa. It has been reported as the third highest burden among neglected tropical diseases (NTDs).² Among the species infecting humans, *S. mansoni* is prevalent in many regions, including North-Western Tanzania. In 2017, the global burden of schistosomiasis was estimated at 1.43 million disability-adjusted life years (DALYs).² Children are particularly vulnerable due to frequent exposure to contaminated water during play and daily activities.¹ Other groups at increased risk include fishermen, women, and peasants, and

this is due to high contact with contaminated water. Chronic infections lead to poor school attendance and poor academic performance, which may be associated with the illness itself or morbidities such as anaemia, fatigue,³ and Stunting (impaired growth and development), wasting (low weight-for-height).⁴ These complications have been observed in many field studies in sub-Saharan Africa.^{5,6} The magnitude of intestinal schistosomiasis among school children in North-western Tanzania ranges from 15.1%^{7,8} to 85.2%⁹ and among preschool children is 80.1%.¹⁰

The PZQ belongs to a class of drugs known as anthelmintics. It is the only antischistosomal agent used to treat human schistosomiasis on a large scale for many years. It is administered as a single dose between 40 and 60 mg/kg of body weight, and it works by killing many parasites, including adult *S. mansoni* worms.¹¹

The mode of action is not exactly known at present, but experimental evidence suggests.^{12,13} Indicates PZQ increases the permeability of the

membranes of Schistosome cells towards calcium ions, which increases calcium influx into the worm, resulting in the induction of contraction of the parasites' muscle, leading to paralysis in the contracted state and finally parasite death.¹⁴

Other studies have demonstrated that in addition to impacting voltage-operated Ca^{2+} channels, PZQ may interact with other schistosome molecules, such as myosin regulatory light chain, glutathione S-transferase, and transient receptor potential channels. Following PZQ administration, increased T regulatory type 1 (Tr1) cell differentiation and decreased inflammation were observed, indicating that PZQ promotes immunoregulatory pathways.¹⁵

Despite decades of mass drug administration (MDA) programs using PZQ, concerns about drug resistance and varying efficacy persist. Its efficacy has been variable in different countries.^{16,17} Evidence from Uganda on pre-school children reported a parasitological cure rate of 100.0%.¹⁸ Some studies have reported the decreasing susceptibility of Schistosomes to PZQ.¹⁹ This has made a great need to assess its efficacy in the different age groups of people in different geographical settings to answer the question of PZQ efficacy in clearing CCA among *S. mansoni*-infected people.

Thus, testing the clearance of the antigen produced by the parasite using POC-CCA is of great importance to understand the exact cause of CR variation, if it is due to reduced efficacy of PZQ or the methods used to assess the efficacy after treatment.

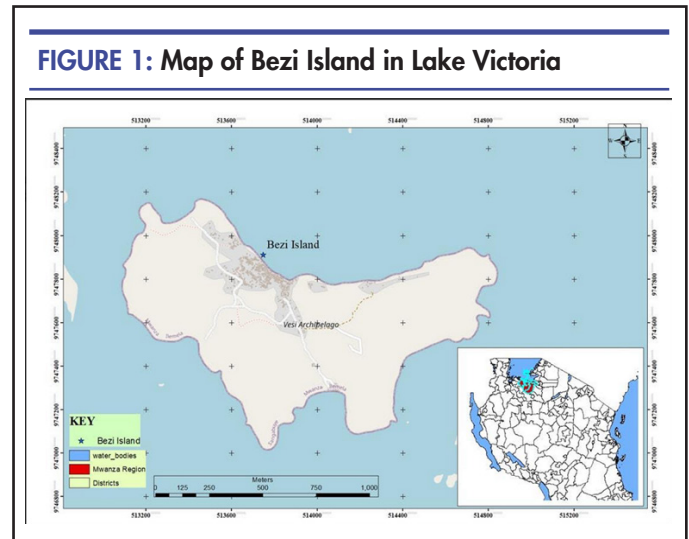
Assessing PZQ effectiveness requires reliable diagnostic tools. While Kato-Katz remains the gold standard, its sensitivity is limited, especially in low-intensity infections. POC-CCA tests offer higher sensitivity but may yield false positives. The CCA is a semi-quantitative method that detects an active *S. mansoni* infection.²⁰ The test detects the CCA released by live juvenile and adult Schistosoma parasites secreted in the host's blood, urine, and milk in female hosts.²¹ The CCA is excreted into the bloodstream as soon as Schistosomules start actively feeding,²² and it is detected in human serum, breast milk, and urine after four weeks post-infection.²³ Understanding the clearance of CCA after treatment is of great importance for evaluating the efficacy of PZQ, which is the key drug for treating schistosomiasis. Furthermore, global knowledge of CCA clearance is appropriate for identifying target groups harbouring persistent active infection, such as egg-negative individuals after treatment.²⁴ This study investigates PZQ efficacy in clearing CCA among pre- and school-aged children in a hyper-endemic area of Tanzania.

METHODOLOGY

Study Area and Population.

This study was conducted at Bezi Primary School, which is located on Bezi Island. Bezi Island is in the Ilemela district in Mwanza region, North-Western Tanzania. The geographical location of the Island is -2.2809092° latitude and 33.1236584° longitude. The area is characterized by a tropical climate, with an annual temperature range of 18 to 28°C, and has a mean annual rainfall of 1068mm. Bezi Island has a population of about 2444 people, where

there is only one primary school and no health facility. Fishing is the major economic activity of the villagers. (Figure 1)



Study Design, Inclusion and Exclusion Criteria

This was a longitudinal study that was carried out between May to October 2021 among 161 school children from one primary school. This study area was selected purposely because there was no data on intestinal schistosomiasis at all. The control measure of schistosomiasis has focused on MDA within the school environment since 2019, and school children have been receiving a single annual round of treatment. The study included pre- and primary school-aged children (2 to 17 years) whose parents/or guardians consented to participate in the study. Participants were excluded from the study if: (i) they had reported a history of adverse reaction to PZQ, (ii). Vomited within 4 hours of PZQ administration.

Sample Size Estimation and Sampling Technique

A longitudinal study was conducted among 161 pre- and school-aged children (2–17 years) from Bezi Island, Mwanza Region, Tanzania. Participants were screened for *S. mansoni* infection using Kato-Katz and POC-CCA tests at baseline and 21 days post-treatment with PZQ (40 mg/kg). Sample size was estimated using a two-proportion formula to detect a 10% difference in sensitivity between the two diagnostic methods, assuming 85% sensitivity for POC-CCA.²⁵ All participants who tested positive (114) at baseline were recruited in the study, and all these were treated with PZQ and monitored at day 21 after treatment.

The total number of pre- and primary school children at Bezi Primary School was 200. Due to this small number, we decided to purposefully include all children at baseline who were willing to participate in our study. Ethical approval was obtained from the joint Ethical and Review Committee of Bugando Medical Centre and Catholic University of Health and Allied Sciences (CREC/495/2021). Informed consent was obtained from guardians, with materials translated into Kiswahili for clarity.

Data Collection Methods

Interview Using a Questionnaire

The principal investigator used a well-structured and pre-tested questionnaire to collect all socio-demographic and clinical information relevant to this study, such as age, gender, and anthropometric measurements (body weight and height) (WHO, 2013); this was done to ensure clarity of the questions in the Swahili language before conducting the study.

Parasitological Examination of Stools Using the Kato-Katz Technique

A single stool sample from each study participant was collected using a labelled stool closed container at baseline and on day 21 after treatment, and from each collected sample, two Kato Katz thick smears were prepared using the Kato Katz technique with a template of 41.7 mg per thick smear.²⁶ The prepared two Kato Katz thick smears were independently examined for *S. mansoni* eggs by two experienced technicians from the National Institute for Medical Research (NIMR) laboratory.

Results interpretation was based on the presence or absence of *S. mansoni* eggs by using microscopy examination. For quality assurance, 15% of all positive and negative Kato Katz slides were re-examined by another independent laboratory technologist who was blinded to the results of the first laboratory technologist.

Parasitological Examination of Urine Using the Point-of-care Circulating Cathodic Antigen Test.

The CCA is a semi-quantitative method of detecting an active *S. mansoni* infection, with antigens released by live adult parasites secreted in the host's urine. A POC-CCA test (Rapid Medical Diagnostic- <http://www.rapid-diagnostics.com/>, batch number 210412036) was used to screen CCA antigen in urine samples. A single urine sample was collected from each of the study participants and tested for CCA antigen based on the manufacturer's instructions (Rapid Medical Diagnostic- <http://www.rapid-diagnostics.com/>), the interpretation of results was based on manufacture instructions (Medical Diagnostic- <http://www.rapid-diagnostics.com/>) which are deep color formed on test line mean strong positive, faint/trace color on test line mean weak positive, no color on test line means negative and no color at test line and control line means invalid results and the test must be repeated. A positive CCA test result (a red band in the control and test windows) on collected urine indicated an active *S. mansoni* infection. All trace results of the test were considered positive. The test was performed by medical laboratory scientists trained in the POC-CCA test who were blinded to Kato Katz results.

Sensitivity, specificity, negative predictive value, and positive predictive value of the tests for the assessment of PZQ clearance were done as demonstrated by AG Lalkhen and A McCluskey.²⁷

Drug Administration and Safety Assessment

All participants with *S. mansoni* infection were treated with a single dose of PZQ (40mg/kg) tablets based on their body weight. Treatment was done under direct observation treatment (DOT) by qualified nurses. Before drug administration, study participants were given food (a piece of bread and one bottle of juice (500ml)) to minimize

the possible side effects of PZQ. Thereafter, a single dose of 40 mg/kg body weight of PZQ was administered to each study participant as recommended by the WHO for the treatment of schistosomiasis.²⁸ Following drug administration, participants remained under direct observation for four hours before leaving the treatment area and were asked to report any side effects to the study team. In case of abdominal pain, symptomatic treatment with paracetamol was offered.

Data analysis

Collected data were entered in a Microsoft Excel spreadsheet for checking for correctness, duplication of responses, and cleaning before being analysed using the R software version 4.2.0 adapt package. Descriptive statistics of socio-demographic and baseline characteristics of the participants were summarized using frequency tables stratified by treatment groups. Disease prevalence was considered based on the number of positive cases by each diagnostic test. A comparison of baseline arithmetic means of egg intensity between light infection intensities (1 ± 99 eggs per gram of feces (EPG), moderate (100 ± 399 EPG), and heavy (≥ 400 EPG). The PCR was defined as a proportion of children who were *S. mansoni* negative at the post-treatment follow-up but were positive at baseline. The ERR was defined as the proportional reduction in the arithmetic mean eggs excreted from baseline to post-treatment and calculated according to the recommended formula by the WHO as times hundred [$1 - (\text{Arithmetic mean egg count after treatment} / \text{Arithmetic mean egg count before treatment})$]. A p-value of < 0.05 was considered statistically significant.

Ethical Approval

The study was approved by the Joint Ethical and Review Committee of Bugando Medical Centre and the Catholic University of Health and Allied Sciences, with ethical clearance number CREC/495/2021, and permission to conduct this study was obtained from the respective district authority. Informed sheets and consent forms were used to obtain guardians' consent for the children to participate in the study and the assent of the children. For each participant/guardian, was given clear description of the study objectives they were asked to use a thumbprint to sign the assent and consent form. All study participants who agreed to participate were asked to collect urine and stool samples for screening for *S. mansoni* infection, and all participants found infected with *S. mansoni* at baseline were treated with PZQ (40 mg/kg) according to the WHO and country guidelines.

RESULTS

Social Demographic Characteristics of Study Participants.

At baseline, a total of 161 study participants were recruited for this study; of these, 90 (55.9%) and 71 (44.1%) were girls and boys, respectively. The overall mean age was 8.0 ± 3.25 years. The majority of the participants were aged between 9 and 11 years, and girls formed a larger proportion than boys, as shown in Table 1 below.

Prevalence and intensity of *S. mansoni* infection at baseline using Kato Katz techniques.

Of the 161 participants, 98 (70.0%) (95% CI: 61.8–77.1) tested positive for *S. mansoni* using Kato-Katz, while

70.8% (95% CI: 62.5–76.8) tested positive using POC-CCA. See [figure 2](#) above. Baseline infection intensities were categorized as light 28 (28.6%), moderate 26 (26.5%), and heavy 44 (44.9%). Post-treatment, the ERR was 73.6%, with a PCR of 66.3% (Kato-Katz) and 27.6% (POC-CCA). Notably, the age group 15–17 achieved a 100% ERR. No statistically significant differences were observed between boys and girls ($p > 0.05$). Based on Kato Katz techniques, the overall prevalence of *S. mansoni* was 98 (70.0%) (95%CI: 61.8 – 77.1). The arithmetic mean egg count was 854.7 ± 1325.1 . The general infection intensity at baseline among study participants were 28 (28.6%) 26 (26.5%) and 44 (44.9%) classified as low/light infection intensity (1 to 99 eggs per gram of feces), moderate infection intensity (100 to 399 eggs per gram of feces) and heavy infection intensity (≥ 400 eggs per gram of feces).

Prevalence and intensity of *S. mansoni* infection at follow-up using Kato Katz techniques

After three weeks of treatment, we observed a decline in infection intensity, as 20 (64.52%) had light intensity, 9 (29.0%) had moderate intensity, and 2 (6.5%) had heavy intensity. However, there was no statistically significant difference in intensity of infection between baseline ($P=0.8$) and follow-up ($P=0.69$) between the age groups ([Table 3](#)).

The heavy infection was higher among girls, 24 (24.5%), than in boys, 20 (20.4%). The age group of 9 to 11 had the highest prevalence of heavy infection, 24 (24.5 %), than other age groups. The prevalence of *S. mansoni* did not differ by age group of the study participants ($p=0.6$) as shown in [Table 2](#).

Prevalence of *Schistosoma mansoni* infection based on Point of care circulating Cathodic antigen test (POC-CCA).

Based on the POC-CCA test, the overall prevalence of *S. mansoni* among study participants was 114 (70.8%) (95% CI: 62.5 – 76.8). There was no sex difference in prevalence of *S. mansoni* based on POC-CCA results ($P=0.55$), though girls had higher prevalence than boys, 62 (54.4%) versus 52 (45.6%) ([Table 4](#)).

The egg reduction rate after 21 days of PZQ administration.

The arithmetic mean at baseline was 854.7 ± 1325.1 , and after treatment, the arithmetic mean declined to 226.1 ± 424.9 , which resulted in an overall ERR of 73.6%. Though it was not statistically significant ([Table 4](#)) between different demographic factors (age and sex). The ERR was higher among males (84.1%) compared to females (67.6%), though it was not statistically significant ($p=0.94$). For age categories, the age group 15 to 17 had 100% ERR compared with other age groups. ([Table 5](#)).

The cure rates among study participants

Assessment of PZQ efficacy for the treatment of intestinal schistosomiasis was done using CR and ERR following the WHO guideline.²⁹ The PCR was defined as a proportion of participants who were *S. mansoni* negative at the post-treatment follow-up but were positive at baseline.

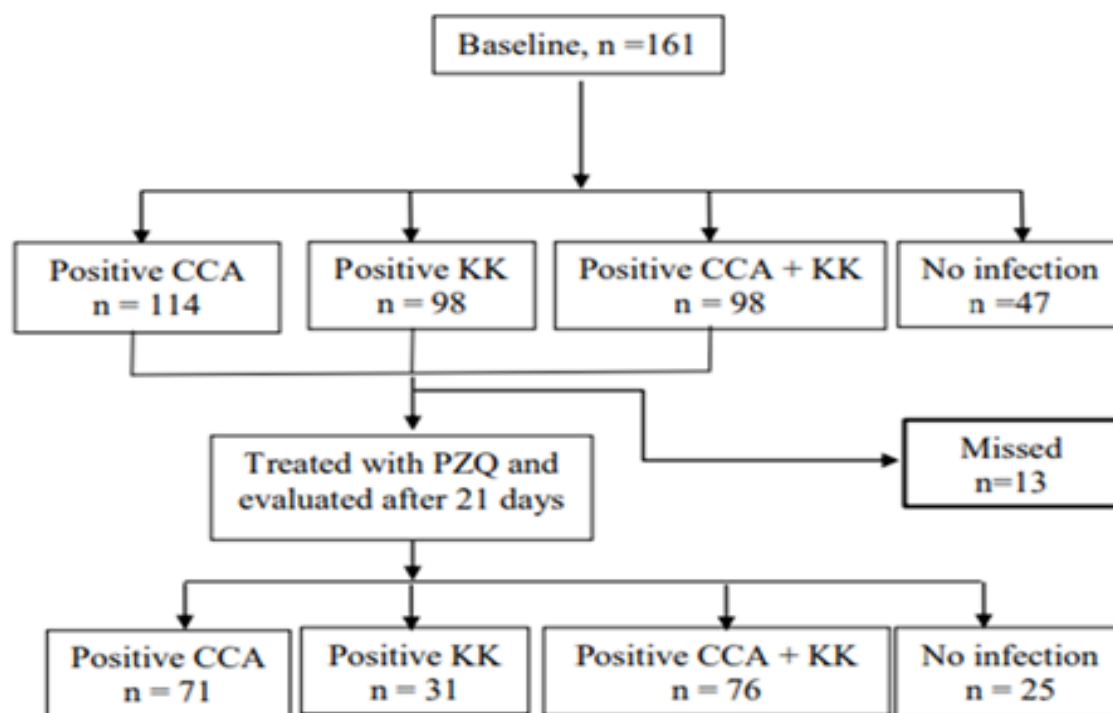
Of the 92 study participants, based on the Kato Katz technique, 61 (66.3%, 95% CI =27-100%) achieved parasitological cure, while 31(33.69%) remained with infection (not cured). Participants in the age group 9-11 were more cured compared with other age groups ([Table 6](#)). Cure rate was higher among Females, 34 (55.7%), when compared to males, 27 (44.3%), though not statistically significant ($p=0.88$) ([Table 7](#)).

The CCA clearance rates based on POC-CCA test were 27.6% (95% CI: 23- 100%). The CR on age characteristics did not vary significantly ($p=0.94$) (see [Table 8](#)). Moderate CR were noted in boys 15 (32.6% than in girls 12 (23.1%), but the difference was not statistically significant ($p=0.41$) ([Table 8](#))

Specificity and sensitivity of the POC-CCA test.

The sensitivity and specificity of POC-CCA tests at baseline were 82.7% and 52.4%, respectively, as compared with the sensitivity and specificity of Kato Katz as the gold standard. The Negative predictive value (NPV) was 56.40%, and the Positive Predictive Value (PPV) of the test was 80.2%. After treatment, the sensitivity, specificity, PPV, and NPV of the POC-CCA test were as follows. [Table 09](#) summarizes the findings.

TABLE 1: Age and Sex Socio-demographic Information of School Children who Participated in the Study at Bezi Island			
Age Categories	Sex, n (%)		Fisher's Exact P-values
	Boys	Girls	
2 – 5	18 (25.4)	24 (26.7)	0.01
6 – 8	20 (28.2)	23 (25.6)	
9 – 11	18 (25.4)	38 (42.2)	
12 – 14	11 (15.5)	2 (2.2)	
15 – 17	4 (5.6)	3 (3.3)	

FIGURE 2: Study Profile Showing *S.mansoni* Infection among pre and Primary School Children at Baseline and at Day 21 of Post PZQ Treatment**TABLE 2: Socio-Demographic and Infection Intensity at Baseline among Participants**

Age Category	Infection Intensity, n (%)			Total (%)	Fisher's Exact <i>P</i> -value
	Low	Moderate	Heavy		
2 – 5	4 (30.7)	4 (30.7)	5 (38.4)	13 (13.3)	0.3549
6 – 8	9 (33.3)	7 (25.9)	11 (40.7)	27 (27.6)	
9 – 11	10 (24.4)	7 (17.1)	24 (58.5)	41 (41.8)	
12 – 14	4 (30.8)	6 (46.2)	3 (23.1)	13 (13.3)	
15 – 17	1 (25)	2 (50)	1 (25)	4 (4.1)	

TABLE 3: General Infection Intensity Before and After Treatment among Participants

Variables	Baseline	Percentage	χ^2	<i>P</i> – value	Follow up	Percentage	Fisher's exact <i>P</i> -value
Light	28	28.5	49.0	0.78	20	64.5	0.69
Moderate	26	26.5			9	29.0	
Heavy	44	44.9			2	6.5	

TABLE 4: Sex and Age Distribution and Prevalence Based on POC-CCA

Age group and Sex	Positive, n (%)	Negative, n (%)	Fisher's exact <i>P</i> -value	
2 – 5	24 (57.1)	18 (42.9)	0.063	
6 – 8	9 (33.3)	21 (29.6)		
9 – 11	34 (79.1)	9 (20.9)		
12 – 14	43 (76.8)	13 (23.2)		
15 – 17	10 (76.9)	3 (23.1)		
Male	62 (54.4)	28 (59.6)	χ^2 0.36	<i>P</i> - Value 0.55
Female	52 (45.6)	19 (40.4)		

TABLE 5: Arithmetic Mean Egg Count at Baseline and Follow-up with their ERR

Age & Sex	Baseline Egg Count (Mean $\pm$ SD)	Kruskal chi-square (χ^2)	<i>P</i> -value	Follow-up egg count (Mean $\pm$ SD)	Kruskal chi-square (χ^2)	<i>P</i> -value	ERR (%)
2 – 5	354.00 $\pm$ 272.50	0.89	0.65	78.00 $\pm$ 94.74	0.01	0.39	51.04
6 – 8	1324.80 $\pm$ 2084.73			72.00 $\pm$ 211.82			61.59
9 – 11	957.88 $\pm$ 1079.53			36.00 $\pm$ 95.68			90.26
12 – 14	465.60 $\pm$ 533.45			81.00 $\pm$ 191.73			62.23
15 – 17	488.00 $\pm$ 349.72			0.00 $\pm$ 0.00			100
Male	945.45 $\pm$ 1616.46	0.21	0.65	69.82 $\pm$ 195.20	0.01	0.94	84.08
Female	931.58 $\pm$ 1134.87			39.16 $\pm$ 91.93			67.64

TABLE 6: Cure Rates Based on the Kato Katz Test Categorized by Age

Age Category	Cured, n (%)	Not Cured, n (%)	Fisher's Exact <i>P</i> -values
2 – 5	6 (9.8)	4 (12.9)	0.88
6 – 8	18 (29.5)	12 (38.7)	
9 – 11	27 (44.3)	12 (38.7)	
12 – 14	7 (11.5)	3 (9.7)	
15 – 17	3 (4.9)	0 (0.0)	
Total	61 (100)	31 (100)	

TABLE 7: Cure Rates Based on the Kato Katz Test Categorized by Sex

Sex	Cured, n (%)	Not Cured, n (%)	χ^2	<i>P</i> - Value
Male	27 (44.3)	15 (48.4)	0.02	0.88
Female	34 (55.7)	16 (51.6)		

TABLE 8: The CCA Clearance Rates Based on the POC-CAA Test Categorized by Age and Sex

Age group and Sex	Cured, n (%)	Not Cured, n (%)	Fisher's exact P-value	
2 – 5	4 (14.8)	9 (12.7)	0.94	
6 – 8	9 (33.3)	21 (29.6)		
9 – 11	10 (37.0)	32 (45.1)		
12 – 14	3 (11.1)	7 (9.8)		
15 – 17	1 (3.7)	2 (2.8)		
			χ^2	<i>P - Value</i>
Male	15 (32.60)	31 (67.39)	0.68	0.41
Female	12 (23.1)	40 (76.9)		

TABLE 9: Sensitivity and Specificity of POC-CCA Test Before and After Treatment with Praziquantel

POC – CCA Test	Before Treatment	After Treatment
Sensitivity	82.7 %	77.8%
Specificity	52.4%	29.8%
Positive Predictive Value (PPV)	80.2%	34.4%
Negative Predictive Value (NPV)	56.4%	73.9%

DISCUSSION

In the present study, we assessed the efficacy of PZQ drug in clearing the Circulating Cathodic antigen by measuring CCA clearance rates by using POC-CCA rapid test and Kato Katz test, and ERR by using Kato Katz test after three weeks (21 days post-treatment with PZQ as recommended by the WHO.²⁹ The CCA clearance rate was assessed by using two different techniques, the Kato Katz technique and POC-CCA, and the ERR was assessed by using the Kato Katz technique alone.

Prevalence and intensity of *S. mansoni* infection

After conducting our study, we observed an overall prevalence of *S. mansoni* to be 70% by using the standard method (Kato Katz), which was slightly lower than 74.9%³⁰ reported from Ethiopia and lower than 80.0% reported at the Ilemela district,³¹ 85.6% reported from the Mara region³² and 81.3% reported from the Wolaita zone in Ethiopia.³³ However, the current prevalence was slightly higher compared to 68.9% reported from a nearby district of Magu,³⁴ 67.6% reported from Ethiopia³⁵ and 63.9% reported from the Ukerewe district.³⁶ Based on the POC-CCA test, the prevalence was 70.8%, which was almost similar to that of the standard (Kato Katz); it was lower than compared of the study from two districts of Ilemela and Magu, which was 94.9%.³⁷ This shows the burden of the diseases and the variations in prevalence and intensity between studies, taking into consideration that our population was heavily infected.

In this study, a single dose of PZQ treatment resulted in a significant reduction in the infection intensity. The Kato Katz technique indeed showed a good reduction of the

infection intensity once we compared the baseline and follow-up results as shown here, at baseline most of the participants 44 (44.9%) had heavy infections, 26 (26.5%) had moderate infection intensity and 28 (28.5%) had low infection intensity. Overall, a small proportion of infected children, 20 (64.5%), remained with light infection, 9 (29.0%) participants remained with moderate infection intensity, and very few, 2 (6.5%), with heavy infection intensity after treatment. We observed that the PZQ drug managed to reduce the infection intensity of *S. mansoni* among infected preschool and school children, hence, it showed a good reduction of mean egg count, which agrees with a report from Tanzania,³⁸ For many years, PZQ has been extensively and repeatedly used in large-scale MDA programs for the control and prevention of schistosomiasis^{3,8}, regardless of the juvenile worms not responding well to PZQ.³⁹ The age group of 15-17 had 100% CR, which can be associated with a known factor of having a high immune status compared with other age groups.⁴⁰

Egg reduction rate as per Kato Katz techniques.

The ERR was not satisfactory according to the WHO guideline for assessing the efficacy of PZQ against intestinal schistosomiasis, which recommends an ERR of >90%.²⁹ The ERR after treatment, which was observed in the current study, declined to 2.26.1 ± 424.9, which is lower than that⁴¹ reported in Tanzania and the other reported in western Ethiopia³⁵ but higher than that reported in Southern Ethiopia.³⁰ The observed differences in ERR might be associated with the variations in individual infection intensity, genetic diversity of parasites, and immunological factors of the definitive host.⁴²

Cure rates as per Kato Katz techniques

The observed CCA clearance rates recorded in this study were within the WHO-recommended ranges of 60–90% for *S. mansoni* infection⁴³. However, the observed CR was slightly higher than 60.9% reported from Côte d'Ivoire and lower than 68.6% reported from Tanzania,⁴¹ 69% reported from Cote d'Ivoire at 21–25 days follow-up⁴⁴ and vary more than 92.6% from the Mwea province report in Kenya,⁴⁵ 80.9% reported from Western Ethiopia.³⁵ And 73.6% in Wondo Genet, Southern Ethiopia.³⁰ The observed variation can partly be explained by the difference in time used to evaluate the efficacy of the drug.⁴⁶ Also number of PZQ doses administered⁴⁷ and the dose (40mg/kgbw versus 60mg/Kgbwt).⁴⁸

This slightly reduced cure rate of PZQ may be associated with the increased number of MDA rounds⁴⁹ among school children. The MDA program should involve follow-up after drug administration, which can help the early detection of drug tolerance or resistance. To date, there is no approved drug by the WHO as an alternative drug to treat or control intestinal schistosomiasis^[38] and this gap needs to be filled. Increasing the monitoring of PZQ efficacy by using different techniques in endemic countries is of great need to monitor the praziquantel efficacy, hence it has been used in treatment and prevention, and control programs.

CCA clearance rates as per POC-CCA test.

In this study, the CCA clearance rates were very low compared with the CR range of 60–90% for *S. mansoni* infection recommended by WHO.⁴³ The observed cure rate was higher than 18% reported from Côte d'Ivoire⁵⁰ and 2.3% reported from North-Western Tanzania.⁵¹ Most of the study participants remained positive (uncured), 21 days post-praziquantel treatment. Participants in the age group of 9–11 were more cured compared with other group ages, this can be associated with the large number of infected participants found at baseline, the CR in heavy infected participants was high from 44 (44.9%) at baseline to 2(6.5%) after 21 days treatment. The factor of reinfection is rarely considered as a source of new infection for those who remained positive after treatment since the stool and urine examination were examined at three weeks post-drug administration (21 days), as recommended by the WHO^[29], the development of the cercaria after skin penetration to adults *Schistosoma* takes 7–8 weeks, this makes the possibility of reinfection to be of minimal consideration.⁵²

The observed difference in cure rate of the Kato Katz techniques and POC-CCA test may be associated with PZQ treatment, the adult worms may paralyze and fail to produce the eggs, but are still alive and can recover later^[51]. Thus, for that reason, the Kato Katz technique will miss the eggs and indicate negative while the worms are still alive and can be detected by the POC-CCA test, which detects the live and active feeding worms. Also, the POC-CCA test detects the antigens/molecules produced by both adult and juvenile worms, while the Kato Katz technique detects only eggs produced by an adult worm. PZQ affects the adult worms and not the juvenile worms.⁵¹ Thus, it is possible that the drug managed to kill the adult's worms that is why we observed a decrease in

eggs production hence high cure rate of Kato Katz test compared to that of POC-CCA test which can be affected by the presence of juvenile which continues to release the CCA into the blood circulation and this can explain the differences in the efficacy of the drug as assessed by the two tests.

Some weaknesses of the POC-CCA method are that it can't be detected until the threshold level is reached.⁵³ It has been reported that the presence of significant variation in sensitivity and specificity exists in some versions of the POC-CCA kit, with buffer or without buffer⁵⁴ and possible cross reactions of other Helminths, Haematuria, presence of Leukocytes, and /or Nitrate in the urine sample have been reported to cause a false positive reaction⁵⁵. For the Kato Katz technique, it depends more on the infection intensity; hence, in lower intensity, it is very difficult to detect the presence of eggs until the number of thick Kato Katz slides per sample is increased.

This study demonstrates that PZQ administered at 40 mg/kg effectively reduced *S. mansoni* infection intensity, with a 73.6% egg reduction rate. However, the low CCA clearance rate (27.6%) suggests persistent active infections despite negative Kato-Katz results. These discrepancies underscore the importance of combining diagnostic methods to accurately assess PZQ efficacy. Potential factors influencing these findings include variations in parasite genetic diversity, host immunity, and reinfection rates.

Sensitivity and Specificity of POC-CCA test.

The sensitivity and specificity of POC-CCA tests varied at baseline and follow-up. These findings show good sensitivity, but the specificity is unsatisfactory. The findings are supported by a previous similar study from Mwanza.⁹ The decrease in sensitivity and specificity at follow-up indicates the reduced ability of POC-CCA to detect the true positive or true negative CCA antigen in the low infection intensity.⁹ The low specificity of the test may indicate a failure of the test to indicate the true negative participants and group them into a positive group (as a false positive group), this may be associated with some weaknesses of the POC-CCA method, where by it can't detect the antigen until the threshold level is reached and possible cross reactions with other Helminths, Haematuria, presence of Leukocytes and /or Nitrate in urine sample.⁵⁵

CONCLUSION

This study confirms praziquantel's efficacy in reducing *S. mansoni* infection intensity among pre- and school-aged children in North-western Tanzania. However, the low CCA clearance rate highlights the need for improved diagnostic tools and monitoring strategies. We recommend continued use of PZQ in MDA programs, coupled with enhanced surveillance to prevent potential drug resistance.

Strengths

This study used two different diagnostic tests, which can isolate the eggs produced by adult *S. mansoni* and detect the antigens produced by a living *S. mansoni*, and it included the pre-school aged children who are not involved in the program of MDA program in our country.

Two Kato Katz thick smears were prepared per sample using the Kato Katz technique with a template of 41.7 mg per thick smear and were independently examined for *S. mansoni* eggs by two experienced technicians the verified by the blinded third scientist.

Limitations

The study include a relatively small sample size and lack of long-term follow-up; these might have decreased the statistical power of the study findings. Lack of a control group for comparison purposes, which might help to isolate the effect of a specific variable, minimize bias, and ensure accurate conclusions about diagnosis and treatment effectiveness.

Future research should explore alternative and cost-effective diagnostics, approaches, and biomarkers to enhance schistosomiasis control efforts.

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Peer Reviewed

Competing Interests: None declared.

Funding: The study did not receive any funding.

Received: 29 November 2024; **Accepted:** 12 May 2025

Cite this article as Zabron FM, Justine CN, Zinga M, Ruganuzza MD, Leeyio RT, Mueller A, Fuss A, Mazigo DH. Inadequate Clearance of Circulating Cathodic Antigen Following Single-Dose Praziquantel Treatment Among Pre- and School-Aged Children in *Schistosoma mansoni* Hyper-Endemic Areas of North-Western Tanzania. *East Afr Science J*. 2025; 7(1): 116-126. <https://doi.org/10.24248/easci.v7i1.120>

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