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Impact of Praziquantel on Schistosomiasis Infection and the Status of Proteinuria and Hematuria among School Children Living in *Schistosoma mansoni*-Endemic Communities in Northwestern Tanzania

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Abstract

The aim of the study was to assess the effect of praziquantel (PZQ) treatment on hematuria, proteinuria and the status of eGFR following treatment in school children infected with *S. mansoni*. A cohort study among 6 - 13 years old children was conducted in the Lake Zone region of Tanzania to assess *S. mansoni* infection using a circulating cathodic antigen (CCA), Kato Kartz while urine dipstick to screen for urine protein levels and red blood cells. A blood sample was taken for every child to determine creatinine levels and later a status of estimated glomerular filtration rate (eGFR). The prevalence of *S.*

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mansoni infection was 64%, 46%, and 24% at baseline, 6 months, and 1 year respectively using CCA test. There was a 62.5% reduction in *S. mansoni* infection from baseline ($p < 0.001$). By KK test the reduction at 6-month interval was 18%. The prevalence of eGFR < 90 ml/min/1.73 m^2 was zero at six months. There was a 50% reduction in proteinuria and hematuria after 1 year ($p < 0.003$). Persistent proteinuria was associated with red blood cells in urine (OR = 3.5, 95% CI 1.21 - 10.0, $p < 0.020$). This study demonstrates that PZQ leads to significant reductions of *S. mansoni* using CCA test, reductions in proteinuria, and hematuria in school children in Tanzania. There was complete remission in eGFR < 90 ml/min/1.73 m^2 from 3.9% to 0% at 6 months. This suggests that praziquantel is effective, but there is still a need for integrated strategies to minimize reinfections.

Keywords

Impact, *Schistosoma mansoni*, School-Aged Children, Tanzania

1. Introduction

Schistosomiasis is a chronic helminth infection caused by trematodes of the genus *Schistosoma* [1]. It is among the neglected tropical diseases [1]. Schistosomiasis infection is a worldwide public health problem but is particularly problematic in sub-Saharan Africa, where approximately 90% of the infections are found [1] [2]. Both *Schistosoma mansoni* and *Schistosoma haematobium* are highly endemic in Tanzania. Available data indicates that 52% of the population in Tanzania is infected with schistosomiasis [3] [4]. Depending on the species, chronic *S. haematobium* infection is well known to be associated with urinogenital and kidney diseases, while chronic *S. mansoni* infection is associated with hepatosplenic diseases [5] [6] [7] [8]. In the Lake Zone (around Lake Victoria), *S. mansoni* is the most common species, and few studies have reported that it is associated with decreased renal function, proteinuria and hematuria in children and adolescents [4] [9] [10]. *S. mansoni*-related renal morbidity is a result of the disease of the host cell-mediated granulomatous immune response to the antigens of the parasite eggs trapped in the tissue [11] [12]. Studies have demonstrated that the association of *S. mansoni* and renal dysfunction can be explained by the deposition of immune complexes formed by *Schistosoma* antigen and IgG/IgM antibodies in the glomerular basement membrane, leading to glomerulonephritis [13] [14]. Chronic infection of *S. mansoni* in children may lead to long-standing proteinuria, which can eventually cause chronic kidney disease and hypertension later in life [9] [10].To date, PZQ administered at the standard single oral dose of 40 mg/kg body weight is the mainstay drug recommended by WHO for chemo-preventive therapy [15] [16] [17]. Mass drug administration (MDA) using praziquantel (PZQ) for schistosomiasis is the main approach adopted by the Tanzania Ministry of Health to reduce schistosomiasis-related

morbidity in school-age children, who have the highest risk of infection [4]. Studies in areas with a high prevalence of *S. haematobium* have shown that double dose administration of PZQ decreases the intensity of infection significantly [9] [10] [18]. Other studies in Africa have demonstrated the effect of PZQ treatment in reducing the prevalence of hematuria and proteinuria [4] [9] [10]. However, to our knowledge, no study has assessed the impact of PZQ treatment on the glomerular filtration rate, proteinuria and haematuria in school children living in intestinal schistosomiasis endemic areas. In that context, the objective of the current study was to determine the Prevalence of *S. mansoni* infection and the impact of repeated doses of PZQ on the glomerular filtration rate, proteinuria, hematuria, and schistosomiasis infection in school children in Mwanza, Tanzania.

2. Method

2.1. Study Area and Population

The study was conducted at Kayenze, Sangabuye and Kabangaja of Ilemela district, from January 2017 to March 2018. Ilemela district has the largest population among all districts in the Mwanza region, and its population increased by 29.5% from 2002 to 2012 (Tanzania population's census 2012). Kayenze, Sangabuye and Kabangaja village were purposely selected to be involved because of the geographical location along the Lake Victoria shorelines and these villages are known to be highly endemic to *S. mansoni* infection [4]. The main source of income for these communities is fishing and farming [4].

2.2. Study Design

This was a prospective cohort study conducted among school children in three wards from 2017 to 2018. The schools and villages were purposely selected based on their location along the Lake Victoria shore. School children were selected by systematic sampling using the class register as a sampling frame. The procedure was done carefully to ensure age and gender representation in the study. School children aged 6 to 13 were included at baseline and then followed up at 6 months and at one year. Study visits occurred at baseline, 6 months, and 1 year. At the baseline visit, all participants with positive CCA were given a single standard dose of 40 mg/kg of PZQ (National guideline) [19]. The same dose was repeated at 6 months and 1 year follow up when the participants tested positive for *S. mansoni* infection using CCA and four-slide Kato-Katz at each point.

2.3. Sample Size Calculation & Sampling Procedure

Our sample size was 400. We calculated the sample size using the Yamane Taro formula (1967) $n = N/1 + N(e)^2$ [20], where n is the sample size, N is the population size of all standard II pupils in the district (94,000), and e is the level of precision at a 95% confidence level, and $p = 0.05$ is assumed for the equation but we added 26% to account for predicted loss to follow up/non-response. Thus, the total sample size was 507 at the baseline.

2.4. Data Collection

A questionnaire was used to collect socio-demographic data, age, gender, history of lake water contact, source of water, history of using PZQ, and clinical data such as edema at baseline, six months, and one-year follow up. The study team adopted this study tool and carried out a pre-test for refinement [18]. Trained research assistants and laboratory technologists collected the data. The parents provided written informed consent.

2.4.1. Anthropometrics Measurements

Anthropometric measurements were taken at each study visit. Participant height and weight were measured using a portable stadiometer and digital weighing scale. Specifically, participants' barefoot stature and weight with minimum clothing and without shoes were recorded to the nearest 0.1 cm and 0.1 Kg, respectively. The nutritional status of each child was calculated using the WHO 2013 BMI percentile charts according to the child's age and sex [21]. Body Mass Index (BMI) was used as the index of choice to assess recent undernutrition as recommended by WHO [22] [23]. Blood pressure was measured using an automatic blood pressure monitor with a cuff size of 9 × 18 cm (USA). Blood pressure was measured while the child was sitting, with their arm at the level of the heart, with the back supported and feet uncrossed on the floor [24]. Three separate readings of the BP at least 10 - 15 min apart were measured and averaged afterward. Blood pressure status was classified according to systolic blood pressure (SBP) and diastolic blood pressure (DBP) percentiles [24] [25].

2.4.2. Proteinuria and Hematuria Measurement

Proteinuria and hematuria were recorded at each study visit. Early morning urine was used to measure proteinuria using urine dipsticks (Multistix™, Bayer, Germany), and proteinuria level was reported as negative, 1+ (30 mg/dL), 2+ (100 mg/dL), 3+ (300 mg/dL), or 4+ (1000 mg/dL) as per manufacturer instructions. Participants were considered to have proteinuria if they had 2+, 3+, or 4+. Hematuria was reported as negative, 1+, 2+, 3+. A score of 2+, or 3+, was considered positive for hematuria.

2.4.3. Examination of *Schistosoma mansoni* and *Schistosoma haematobium* by Urine Sample

A single early morning urine sample was collected from each participant at baseline, six months and one-year follow up to screen for *S. mansoni* infection. The urine POC-CCA Cassette test was performed according to the protocol and procedures described by the manufacturer (Rapid Diagnostics, Pretoria, South Africa batch number; 170331037). POC-CCA test results were recorded on four-point scales: Negative, positive 1, positive 2, and positive 3. Participants with positive 1 to 3 were considered to have *S mansoni* infection. To detect *S. haematobium* infections, 20ml urine was filtered through a syringe filter with 20 μm mesh size (Millipore Art. No. NY2002500), and filters were examined by microscopy for the presence of *S. haematobium* eggs [26] [27].

2.4.4. Stool Collection and Microscopic Examination

Four Kato-Katz thick smears were prepared from different parts of the single stool sample using a template of 41.7 mg (Vestergaard Frandsen, Lausanne, Switzerland) [28] [29] [30]. Following standard protocol, then the Kato smears were arranged in wooden slide boxes, packed together in large container boxes, and transported to the National Institute for Medical Research (NIMR) laboratory, Mwanza Research Centre, where they were examined after 24 hours for *S. mansoni* eggs by two experienced laboratory technicians. The intensity (eggs per gram (epg) of faeces of *S. mansoni* infection) was calculated as an average egg per gram of faeces for all the four Kato smears prepared for each child. We used a template delivering 41.7 mg of stool to prepare Kato slides, the eggs of each parasite in the slide were counted, and the number of eggs was multiplied by 24 to calculate epg for *S. mansoni* infection. *Schistosoma mansoni* intensities were categorized as per WHO intensity classes as light (1 - 99 epg), moderate (100 - 399 epg), and heavy (≥400 epg) [28] [29] [30] [31]. For quality assurance, 10% of the negative and positive Kato-Katz thick smears were re-examined by a third technician. One school was chosen to look at the intensity of egg and infection reduction rate among the children, who had schistosomiasis, and this was done at 6 months and 1 year follow up this was done for checkup purpose only.

2.4.5. Examination of Creatinine Level in Serum

Serum creatinine level was measured using a Cobas 400 clinical chemistry machine (Roche, Germany), calibrated by the Creatinine Jaffe 2 method. An estimated glomerular filtration rate (eGFR) was calculated using the modified Schwartz equation (taking into account estimation of GFR in children using serum creatinine and height) as recommended by the Kidney Disease Improving Global Outcomes (KDIGO) guidelines and validated in children with and without CKD [32]. This was done for all participants at baseline and at 6 months and 12 months only for participants with eGFR below 90 at baseline.

2.5. DATA Management and Analysis

The data were captured in Microsoft excel 2010 and then exported into STATA Version 15 (Stata Corp, Texas, USA) for data cleaning and analysis. Frequency and percentages were used to describe socio-demographic and clinical characteristics at baseline, six and twelve months. To estimate factors assorted with *S. mansoni* infections and renal dysfunction indicators (proteinuria and hematuria) at baseline, 6 and 12 months. We used bivariate and Multivariable Logistic regression analysis.

3. Results

3.1. Baseline Characteristics of the Study Participant

The total number of children in the three schools was 840, and after considering inclusion criteria, 507 were eligible. Of the 507 enrolled, 84% (427/507) completed the 6 months follow up, and 80% (406/507) completed the 1-year follow

up. Of the 101 children who didn't complete the 6 month and 1-year follow ups, 79 were lost to follow up, 11 failed to get urine samples, and 11 had missing data (Figure 1). All the participants who were lost to follow up were included in the final analysis when comparing outcomes of *S. mansoni* infection between those who lost to follow up and those who did not.

Fifty-two percent of the 406 who completed the follow up were female (n=), >72% reported that lake or pond water was their main water source, and > 88% had contact with the lake in the past one week prior to the study (Table 1).

Kato-Katz thick smears were performed at six months for Kayenze primary school participants, and the results show an 18% reduction in heavy infections at one year follow up.

3.2. Prevalence of *S. mansoni* and Its Associated Factors at Baseline, Six Months and One Year Follow up

Figure 2 shows prevalence of *S. mansoni* infection at baseline, six months and one year using CCA test. A standard single-dose of PZQ 40 mg/kg was given at baseline and repeated at six months. Prevalence at baseline was 64.3%, at six months was 46.4% and at one year, follow up was 24.1% respectively. This reduction was statistically significant $p < 0.001$. When comparing the prevalence from baseline to one year, there was a higher prevalence of *S. mansoni* infection for those who did not complete follow by 51% as compared to those who completed the follow up 24% in one year. Kayenze primary school had a high prevalence of

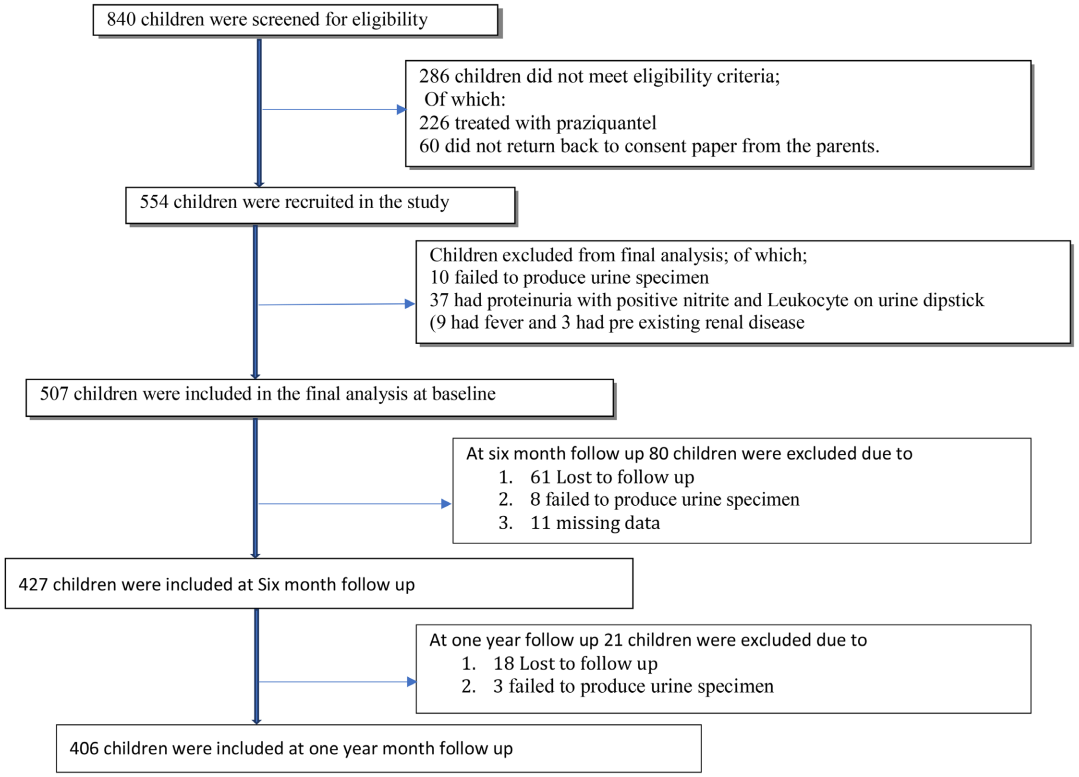


Figure 1. Study enrollment overview.

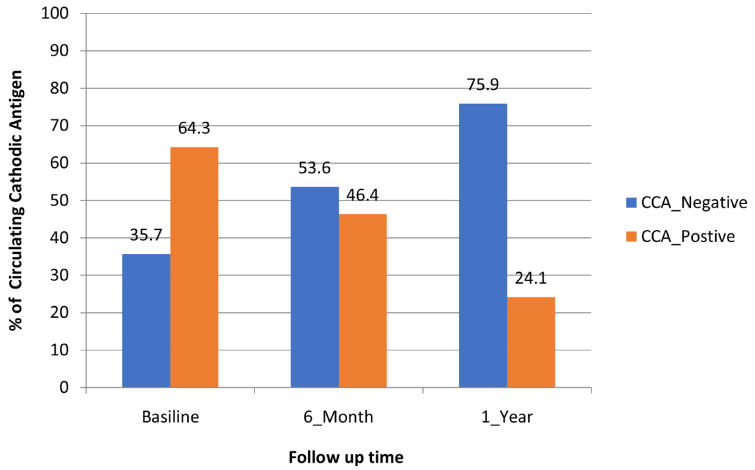


Figure 2. Prevalence of *S. mansoni* at baseline, six month and one year follow up by Circulating Cathodic Antigen.

Table 1. Social demographic characteristics.

	Follow up time	
	6 months (n = 427)	**12 months (n = 406)**
	n (%)	**n (%)**
Age (years)		
≤9	320 (74.94)	180 (44.33)
≥10	107 (25.06)	226 (55.67)
Gender		
Female	225 (52.7)	213 (52.5)
Male	202 (47.3)	193 (47.5)
Type of water source		
Lake or pond water	314 (73.5)	293 (72.2)
Tap water	113 (26.5)	113 (27.8)
Contact with lake in the past 1 week		
Yes	383 (89.7)	361 (88.9)
No	44 (10.3)	45 (11.1)

S. mansoni by CCA and was selected for follow up of infection intensity. Kato-Katz thick smears were performed at six months for Kayenze primary school participants, and the results show an 18% reduction in heavy infections at one year follow up. The intensity of *S. mansoni* infection, categorized as light, moderate, and heavy was 19.6% (19/179), 13.4% (24/179), 44.7% (80/179) at 6 months and 10.7% (19/178), 14.0% (25/178), 36.5% (65/178) at 1 year follow up. Severe nutritional status was the only factor associated with *S. mansoni* infection at baseline in multivariate analysis (OR [95% CI] 0.39 [1.22 - 8.87], p = 0.019) (Table 2(a) and Table 2(b)).

Table 2. (a) Factors associated with *S. mansoni* at baseline; (b) Factors associated with *S. mansoni* at 6 months and 12 month follow up status.

(a)

BASELINE						
	S. mansoni		Univariate		Multivariate	
Factor	Positive n (%)	Negative n (%)	cOR [95% CI]	p value	aOR [95% CI]	p value
Age (Years)						
≤9	251 (62.28)	152 (37.72)	1		1	
≥10	75 (72.12)	29 (27.88)	1.56 [0.97 - 2.51]	0.063	1.27 [0.77 - 2.09]	0.333
Sex						
Female	160 (62.99)	94 (37.01)	1		1	
Male	166 (65.61)	87 (34.39)	1.12 [0.77 - 1.61]	0.538	1.08 [0.74 - 1.56]	0.689
Water Source						
Tap	125 (61.58)	78 (38.42)	1		1	
Lake Water	201 (66.12)	103 (33.88)	1.22 [0.84 - 1.76]	0.296	1.31 [0.86 - 1.99]	0.212
Contact to lake within 1 week						
No	125 (61.58)	78 (38.42)	1		1	
Yes	201 (66.12)	103 (33.88)	0.90 [0.54 - 1.49]	0.692	0.81 [0.46 - 1.44]	0.490
Nutritional Status						
Normal	248 (60.93)	159 (39.07)	1		1	
Moderate	49 (74.24)	17 (25.76)	1.84 [1.02 - 3.32]	**0.040**	1.76 [0.98 - 3.18]	0.600
Severe	29 (85.29)	5 (14.71)	3.71 [1.41 - 9.81]	**0.008**	3.29 [1.22 - 8.87]	**0.019**

(b)

FOLLOW UP STATUS								
	6 Month				12 Month			
	Univariate		Multivariate		Univariate		Multivariate	
Factor	**cOR [95% CI]**	**p value**	**aOR [95% CI]**	**p value**	**cOR [95% CI]**	**p value**	**aOR [95% CI]**	**p value**
Age (Years)								
≤9	1		1		1		1	
≥10	0.72 [0.46 - 1.11]	0.139	1.76 [0.48 - 1.89]	0.224	0.92 [0.58 - 1.45]	0.717	0.92 [0.57 - 1.47]	0.739
Sex								
Female	1		1		1		1	
Male	0.77 [0.53 - 1.14]	0.195	0.78 [0.53 - 1.14]	0.202	0.82 [0.52 - 1.30]	0.405	0.80 [0.50 - 1.27]	0.346

Continued

Water Source								
Tap	1		1		1		1	
Lake Water	1.01 [0.66 - 1.57]	0.930	1.08 [0.67 - 1.75]	0.741	0.73 [0.45 - 1.20]	0.222	0.63 [0.37 - 1.10]	0.091
Contact to lake within 1 week								
No	1		1		1		1	
Yes	0.85 [0.46 - 1.59]	0.610	0.77 [0.38 - 1.54]	0.461	0.13 [0.61 - 2.82]	0.498	1.71 [0.74 - 3.93]	0.210
Nutritional Status								
Normal	1		1		1		1	
Moderate	1.11 [0.55 - 2.25]	0.759	1.11 [0.55 - 2.26]	0.766	0.78 [0.37 - 1.65]	0.529	0.74 [0.35 - 1.57]	0.431
Severe	3.71 [1.41 - 9.81]	0.097	4.47 [0.21 - 1.08]	0.076	0.55 [0.22 - 1.35]	0..192	0.53 [0.21 - 1.33]	0.176

3.3. Laboratory Results for eGFR and Proteinuria Status

In this study, at baseline, 57 out of 507 participants had 1.6% and 3.9% severe to moderate decrease in eGFR of less than 60 and 90 respectively. During follow up at six months, all 57 participants with eGFR of below 90 had complete remission.

The prevalence of proteinuria (14.0% at baseline, 13.1% at 6 months and 8.8 % at 1 year) showed a statistically significant (p-value 0.003) decrease at points in the follow up (Figure 3(a)).

3.4. Laboratory Results for Blood in Urine (Hematuria) and Renal Dysfunction Status

At baseline, 7.3% (37/507) of participants had hematuria of 2+ to 3+. The same level of hematuria was found in seven out of 427 (7/427) participants at six months and eighteen out of 406 (18/406) at one year follow up (Figure 3(b)). Reinfections could have contributed to the increase in number from six months to one year. Overall renal dysfunction decreased from 22.9% at baseline to 13.3% at one year follow up.

3.5. Factors Associated with Persistence Proteinuria

Factors associated with the persistence of proteinuria in multivariable analysis were the presence of blood in urine and contact with a lake within one week. Children with hematuria had three times higher odds of having persistent proteinuria compared to those without blood in their urine (OR [95% CI] 3.48 [1.21 - 9.98], p = 0.020) (Table 3).

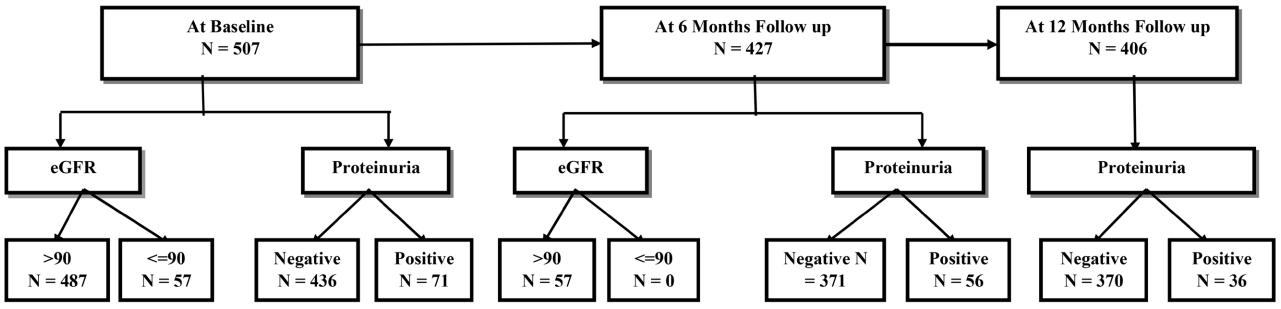
4. Discussion

We conducted a cohort study to investigate the Impact of Praziquantel on the treatment of schistosomiasis infection as measured by Circulating Cathodic Antigen (CCA) test, KK test and status proteinuria and hematuria among school

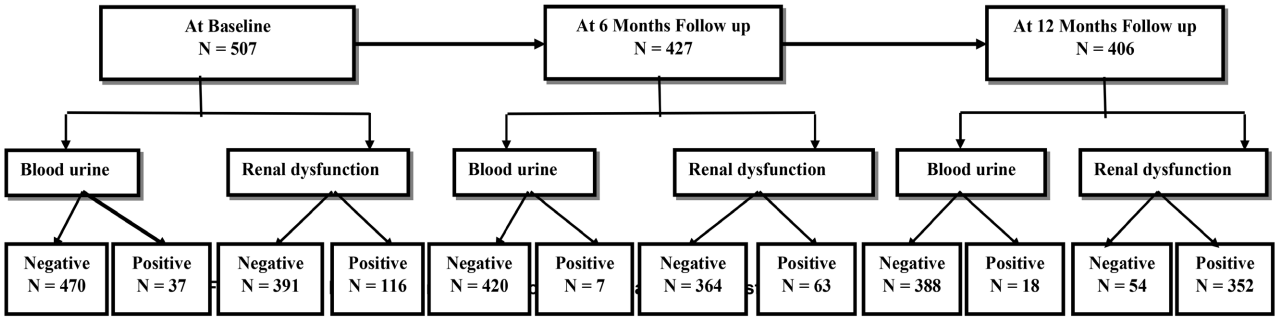
children living in Ilemela district of region Mwanza, Northwestern Tanzania, an endemic area for *Schistosoma mansoni*. Our main findings indicate that; with three rounds of single-dose 40 Mg/Kg per body weight Praziquantel, there was a 62.5% reduction in the rate of *Schistosoma mansoni* infection between baseline and one year of follow up using CCA test. This shows *S. mansoni* continue to be public health importance in this setting. Also, all those with a baseline eGFR less than 90 had complete resolution at 6 months follow up and proteinuria reduction from 14% at baseline to 8.9% at 1 year follow up. The prevalence of hematuria dropped from 7.3% to 4.4% at one year. Overall, renal abnormalities decreased from 22.9% at baseline to 13.3% at 1 year of follow up.

Table 3. Factors associated with persistence proteinuria at 6 months and 12 months follow up.

	FOLLOW UP STATUS							
	6 Month				12 Month			
	Univariate		Multivariate		Univariate		Multivariate	
Factor	cOR [95% CI]	p value	aOR [95% CI]	p value	cOR [95% CI]	p value	aOR [95% CI]	p value
Age (Years)								
≤9	1		1		1		1	
≥10	0.76 [0.39 - 1.51]	0.437	0.79 [0.39 - 1.55]	0.746	1.13 [0.56 - 2.25]	0.736	1.10 [0.61 - 2.00]	0.743
Sex								
Female	1		1		1		1	
Male	1.07 [0.80 - 1.90]	0.804	1.10 [0.62 - 1.96]	0.746	1.26 [0.63 - 2.50]	0.510	1.01 [0.56 - 1.80]	0.994
Water Source								
Tap	1				1			
Lake Water	0.82 [0.44,1.52]	0.523			0.66 [0.32 - 1.34]	0.248		
Contact to lake within 1 week								
No	1		1		1		1	
Yes	0.33 [0.16 - 0.70]	0.04	0.34 [0.16 - 0.71]	0.004	0.27 [0.12 - 0.61]	**0.002**	0.36 [0.17 - 0.76]	**0.007**
Schistosomiasis by CCa								
No	1				1			
Yes	1.02 [0.58 - 1.81]	0.94			1.23 [0.57 - 2.66]	0.593		
RBCs in Urine								
No	1				1		1	
Yes	2.61 [0.49 - 13.80]	0.259			4.48 [1.48 - 13.24]	**0.008**	3.48 [1.21 - 9.98]	**0.020**
Nutritional Status								
Normal	1				1			
Moderate	0.28 [0.15 - 0.05]	0.153			0.48 [0.10 - 2.30]	0.363		
Severe	0.45 [0.40 - 0.07]	0.399			0.69 [013 - 3.68]	0.661		



(a)



(b)

Figure 3. (a) Flow chart for Laboratory results in eGFR and Proteinuria; (b) Flow chart for Laboratory results in Blood in urine and Renal dysfunction status.

Currently, the focus of the Tanzania Ministry of Health, Community Development, Gender, Elderly and Children on schistosomiasis control is preventative chemotherapy for school-aged children from 6 - 16 years as this category has the highest risk of infection [4] [29] [33]. Mass drug administration (MDA) of PZQ for schistosomiasis is the main approach adopted by the World Health Organization by the Tanzania national schistosomiasis control program to reduce related morbidity in school children. PZQ is the drug of choice for the treatment of schistosomiasis and is safe and efficacious in children [31]. Our results at one year of follow up with three rounds single-dose PZQ given at baseline, six months, and one year shows a 62.5% reduction in *Schistosoma mansoni* infection. This reduction is slightly low compared to other studies done in Africa [33] [34]. The nature of the study methodology can explain this difference. We used an intention-to-treat protocol where we followed routine scheduled MDA at baseline, 6months and one year, while others studies were randomized control trials, with single or double doses at 8 to 10 weeks [35] [36] . But also, Low reduction rate can also be explained by reinfections after treatment, failure of PZQ to kill immature worms which reach maturity after treatment in high transmission settings [37].

Since our population was children and had recurrent exposure, they are likely to have immature worms that were not affected by PZQ and grew to adult worms by the time of subsequent follow up [37] [38].

Also, reinfection can explain the low rate reduction, this study population of

school children as their continuing living in the same environmental exposure.

Persistent proteinuria is recognized as a marker of kidney damage and is a well-known risk factor for progression to chronic kidney disease (CKD) in adults and children [38] [39] [40] [41]. We observed persistent proteinuria reduced by 36% at one-year follow up. This reduction is low compared to other studies done in Africa [38] [42] [43]. The source of this difference is unclear and suggests the need for future research. It has been established that the degree of proteinuria is highly associated with the progression to CKD [44]. Children who present with persistent proteinuria should undergo an evaluation of renal function and a thorough history detailing any significant illness to help determine the possible cause [45] [46]. Blood in urine was strongly associated with the persistence of proteinuria.

Participants with persistent proteinuria had three times higher odds of having red blood cells in urine compared to those without proteinuria. This need further evaluation in clinical practice in children with persistent protein Studies elsewhere in Africa have demonstrated a correlation between proteinuria and hematuria on dipstick tests and the intensity of schistosomiasis infections [42] [43] [44].

Our study has reported persistent hematuria of 40% at one-year follow up. This reduction is low compared to other studies done elsewhere in Africa [5] [7] [44]). The presence of blood in urine is long established as a marker of *S. haematobium* infection, and its presence has been used as a screening tool for urogenital in schistosomiasis in Africa ([44] [46]. This study had a low prevalence of *S. haematobium*, and chances for post-treatment hematuria reduction are low in hematuria caused by *S. mansoni* [47] [48] [49].

We found complete remission of decreased eGFR in this study at six months follow up. It is unclear whether the reduction was related to PZQ used or the remission was because of an acute injury at baseline.

Our study limitations are as follows; the study was done in an area with a high prevalence of *S. mansoni*. This limits the generalization of our results. Gold standard Kato-Katz thick smears for identification of *S. mansoni* were not done to all schools only done to one school with high prevalence of *S. mansoni*; therefore, the results could be compared. With CCA test, this call for further studies in this age group in this area to compare the efficacy of CCA test and KK test.

5. Conclusion and Recommendation

The present study found that the impact of PZQ on *S. mansoni* infection using CCA test and KK test at six month interval was moderate effective in the reduction of the infection; this can be explained by reinfections after treatment, failure of PZQ to kill immature worms which reach maturity after treatment in high transmission settings. Also, the study shows complete remission of decreased eGFR (<90) from 3.9% at baseline to zero at six months of follow up.

Randomized control trials are needed to justify repeated treatments and to in-

clude other control measures such as behavioral change, communication, and improvement in water supplies and sanitation. Further studies are also recommended to determine the precise time for CCA clearance determination for repeated cycles with PZQ.

The study further noticed a low reduction rate of persistent proteinuria and hematuria at one year follow up. We therefore recommend further studies in this risk group to identify other causes of persistent proteinuria and hematuria.

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Author' Contributions

NMK contributed to the study design, data collection and analysis and manuscript preparations, BR, NMK, EM contributed to data analysis and interpretation.HDM, BRK, CM, BW, KR and JB, RP critically reviewed the manuscript and were responsible for interpretation of the results, validation. All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare that they have no competing interests.

Consent for Publication

Permission to publish was obtained from the ethical clearance committee, Catholic University of Health and Allied Sciences, certificate number CREC/121/2016.

Ethical Consideration

The Research Clearance Certificate No: CREC/121/2012 was issued jointly by the Catholic University of Health and Allied Sciences and Bugando Medical Centre in Tanzania. In addition, permission was obtained from Ilemela District Commission, Ward Executive Officers, Village Executive Officers and the Headmasters of Kayenze, Sangabuye and Kabangaja Primary Schools. On behalf of these children, all parents or legal guardians were provided with the Kiswahili written informed consent to allow their children to be recruited in this study and give consent. Additionally, assent was obtained from children aged 7 years to 13 years. For those who agreed to participate in this study, their information was collected by data collectors orally or through a self-administered method. For

confidentiality purposes, all clinical and demographic data from the study participants received codes for identification purposes. All children identify being infected with *S. mansoni* by either CCA test or KK test were treated with PZQ (40 mg/kg) according to WHO recommendation [15] [28]. With additional rounds at 6 month and one year follow up. Our cohort of patients with persistent proteinuria was referred to the nephrology clinic at Bugando Medical tertiary hospital in Mwanza for further investigation and closed follow up.

Availability of Data and Materials

The datasets collected and/or analyzed during the current study are available from the corresponding author upon request.

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