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The Role of Knowledge and Practices in Schistosomiasis Transmission Among Primary School Children in Osun State, Nigeria

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ABSTRACT

Background: Studies have documented various risk factors associated with schistosomiasis infection transmission, but little is known about the influence of knowledge on practices that contribute to the transmission of the infection. This study, therefore, seeks to document the importance of knowledge on practices that contribute to the transmission of schistosomiasis among primary school children.

Methods: This study employed a descriptive study design. A total of 504 primary school children were recruited from three senatorial districts in Osogbo using convenience sampling. Vital information on knowledge of schistosomiasis infection and practices that aid its transmission was collected using a semi-structured interviewer-administered questionnaire. A twenty-one-point knowledge question was used to compute the knowledge score and dichotomized into good knowledge (\geq 10 points) and poor knowledge (<10 points), while sixteen points practice questions were used to compute the practice score dichotomized into good practice (\geq 8 points) and poor practice (< 8 points)

Results: A more significant percentage (93%) of the respondents had poor knowledge of schistosomiasis, although a good number of them (65.1%) exhibited good practice. A little above a third (35.9%) engaged in swimming, while about a fifth (22.8%) engaged in fishing. About a fifth (22.6%) engage in defecation in river water, while very few (4.0%) drink from such polluted water. The logistic regression model revealed that male respondents were 1.6 times more likely to have poor practices than their female counterparts (aOR 1.6, 95% CI 0.413-0.913), those who have received health talk on the infection were 27 times less likely to have poor practices (aOR 0.37, 95% CI 0.175-0.761), those who reported being positive for the infection were 4.4 times more likely to have poor practice (aOR 4.4, 95% CI 1.703-11.260) and those who had poor knowledge of the infection were 6.0 times more like to have poor practices relating to the infection (aOR 6.0, 95% CI 0.014-0.278).

Conclusion: Primary school children have poor knowledge of schistosomiasis, which influences the practices that aid infection transmission. Therefore, public health education is needed to control the infection.

Keywords: Schistosomiasis, Knowledge, Practices, School children, Health talk

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1.0 INTRODUCTION

Urinary schistosomiasis, a parasitic disease highly prevalent in the tropics and sub-tropics, is caused by a parasitic flatworm known as Schistosoma haematobium [1]. It is a neglected parasitic disease that has resulted in several morbidities and mortalities across the world [2]. The disease is widespread in the developing countries of the world, and it's the most socioeconomically devastating tropical infection after malaria [3]. Schistosomiasis transmission has been reported in 78 countries, and estimates have shown that at least 251.4 million people required preventive treatment in 2021[4]. People with strained finances are usually more vulnerable to infection since they cannot afford ideal sanitation facilities, such as modern toilets and potable water for drinking and performing other domestic activities [5]. Schistosomiasis is a behavior-related infection that has been reported in the literature to be significantly associated with specific age groups, genders, and socioeconomic status [6]. Several factors, including poor sanitation, poverty, ignorance, and limited access to and availability of health facilities and social amenities, have been reported to account for the high prevalence of urinary schistosomiasis in developing countries [4]. Humans contract this infection when they come in contact with contaminated water, harbouring the infective stage of the parasites during water-related activities, such as irrigation farming, fishing, laundry, bathing, and swimming [1]. School-age children are the most vulnerable to urinary schistosomiasis due to their high tendency to contact river or stream water, which predisposes them to the infection [7]. It is on this premise that the World Health Organization (WHO) has recommended that when a schistosomiasis prevalence of <10% is observed in a school, praziquantel should be made available in health facilities when prevalence is between 10 to 50%, mass administration of praziquantel should be considered and when it is above 50%, annual mass administration of praziquantel should be carried out [4].

It's a well-known fact that lack of awareness about the mode of transmission of parasitic infections increases the risk of infection. Understanding the social, cultural, and behavioral determinants of infections affects the epidemiology and control of such infections and consequently aids in designing effective control strategies [8,9]. Thus, the role of awareness and knowledge of infection cannot be overemphasized in the context of disease control. Individuals' knowledge about a particular infection goes a long way in determining their behaviors concerning disease prevention choices, and this thus plays a vital role in

the transmission of infections of public health significance [10]. Studies have shown that poor knowledge of transmission modes, symptoms, diagnoses, and preventive strategies affected efforts toward schistosomiasis control [11]. Even in another study where respondents had a high level of awareness of schistosomiasis, poor knowledge of the infection transmission among these subjects was a major challenge in prevention efforts [12]. Studies have documented various risk factors associated with schistosomiasis infection transmission, but little is known about the influence of knowledge on practices that contribute to the transmission of the infection. This study, therefore, seeks to document the role of knowledge in practices that contribute to the transmission of schistosomiasis infection among primary school children.

2.0 METHODOLOGY

2.1 Description of the Study Areas

The study was conducted within the three senatorial districts of Osun State, namely Osun West, Osun East, and Osun Central. The State is projected to have a population of 6.7 million (population projected from 1991 and 2006 censuses by the National Population Census, NPC). The state is divided into three federal senatorial districts, each consisting of ten Local Government Areas (LGAs), which make up a total of thirty LGAs. Osun State is situated in the tropical rainforest zone. It covers an area of approximately 14,875 sq km and lies between latitude 7° 30′ 0″ N and longitude 4° 30′ 0″ E. It has a tropical dry and wet climate. The driest month is January, which has 9mm of rainfall. Osun is a little bit clouded because of the thick vegetal cover. Predominantly, the communities comprise farmers, traders, and skilled workers. A good number of children from the communities attend government primary schools. The schools have well-ventilated classrooms and water and toilet facilities for the sanitary use of the pupils. All the sampled schools have at least a river within a 5 km radius. Community members, including the children in the studied locations, engage in water contact activities such as fishing, swimming, bathing, and block-making.

2.2 Study Design and Population:

This study is a descriptively designed. The study population comprises schoolchildren aged five to sixteen (5-16) in selected communities in Osun State. A good number of the primary six pupils were above the regular 12 years of primary school age, hence the inclusion of children aged 13 to 16.

2.3 Inclusion and Exclusion Criteria

Children who have spent a minimum of six years within the community and who do not have a history of praziquantel usage in the last six months were recruited into the study. Pupils who showed symptoms of sickness and those whose parents did not consent to participate in the study were excluded. Also, pupils in primary one were excluded from this study since they were less than six months in the school at the time of this data collection.

2.4 Sample Size Calculation

Since the number of schoolchildren in the three studied local government areas was confirmed to be more than 10,000 according to the Osun State school deworming program record, Leslie Fisher's formula for calculating a sample size greater than 10,000 was used to estimate the sample size for this study.

$$n = \frac{Z^2 pq}{d^2}$$
Where:

n= sample size; Z= standard deviation; 1.96; p= prevalence: 55.8%; q= 1- p; d= precision; 0.05 [13]

Using the above formula, the sample size needed for the study is 378. The addition of 10% for Attrition makes the sample size equal to 416. Voluntary involvement of an additional 88 students who showed interest in the study increased the sample size to 504.

2.5 Sampling Technique

A multistage sampling technique was adopted. For stage one, one LGA was randomly selected from each senatorial district via simple balloting. For stage two, two consenting primary schools from each LGA and located within a 5 km radius of stream/river were selected following consecutive sampling. For stage three consist of total sampling of consenting students from primary 2 to 6

2.6 School Selection / Characteristics

School selection across the state is presented in Table 1 below. Two consenting schools were conveniently selected from each LGA in a senatorial district. All the schools selected have at least a river within a 1km radius of the school. Schools 6, 7, and 8 can be referred to as a single school, as the three schools are formed from a single mega building.

2.8 Questionnaire Survey

Before questionnaire administration, consent was sought from caregivers and school authorities to enable the pu-

Table 1. School Selection

School code	Proportion of students sampled per school	Senatorial Dis- trict	LGA
1	50 (9.9%)	Osun Central	Ila
2	81 (16.1%)	Osun Central	Ila
4	110 (21.8%)	Osun East	Obokun
5	67 (13.1%)	Osun East	Obokun
*6	40 (7.9%)	Osun East	Ayedaade
*7	19 (3.8%)	Osun West	Ayedaade
*8	30 (5.9%)	Osun West	Ayedaade
9	107 (21.2%)	Osun West	Ayedaade

Schools with * are formed under the same mega budling

pils to participate in the study. Health talks were organized in various schools to enlighten all the stakeholders on the significance of the study. Only children of parents who gave consent were recruited into the study. A pretested interviewer-administered questionnaire was then used to elicit information from the respondents on sociodemographic characteristics, sanitation and hygiene practices, and medical history. Parents's occupations were classified as high-risk and low-risk. High-risk occupations are those directly related to water, such as irrigation, farming, fishing, car washing, etc. In contrast, low-risk occupations do not require stream/river water contact. A twenty-point knowledge questions were used to compute the knowledge score and dichotomized into good knowledge (respondents' score ≥ 10 points) and poor knowledge (respondents' score <10 points). In comparison, 16-point practice questions were used to assess practices and dichotomized into good practice (respondents' score \geq 8 points) and poor practice (respondents' score \leq 8 points). A correct answer was equal to 1, while a wrong answer attracted zero.

Validity of the instrument

The instrument was pretested in a private school in Osogbo using ten percent of the total sample size. All possible errors identified during the pretest were corrected appropriately. Experts in public health also vetted the instrument before it was deployed for actual data collection.

2.9 Definition of Outcome Variables

Twenty-item questions were used to assess students' knowledge, and 10 was considered the average score. The knowledge status of the respondents was determined as good if the respondent scored≥ 10 points in knowledge questions and poor if the score was below 10 marks. 16-item questions were used to assess the respondents' practices, and 8 was considered the average score. Respondents who scored below eight were said to exhibit poor hygiene practices, while those who scored above 8 were

considered to exhibit good hygiene practices.

2.10 Ethical Considerations

Permission and approval were sought from the Ethical Review Committee of Osun State Ministry of Health (OSHREC/PRS/569T/193) and the Planning, Research and Statistics Department of Osun State Ministry of Education (MOE/PRandS/SS 2/vol.vi/43). Participants/ caregivers were informed about the objectives of the study. This was facilitated through an organized meeting between parents, school management, and the research team. Signed consent was obtained from the caregivers. Participation was voluntary to respect people's integrity.

2.11 Statistical Analysis

All results from the field were coded, compiled, and recorded correctly in a prepared form. This was done daily to forestall the occurrence of missing data. Using SPSS version 25.0, Descriptive statistics (proportion, means, standard deviation, and frequency tables) were used to summarize the data. The chi-square test was used to test the association between categorical variables. Multivariate analysis using logistic regression was used to determine factors associated with poor practice. Adjusted odds ratios and their 95% confidence intervals were reported. Values less than 0.05 were considered statistically significant.

3.0 RESULTS

3.1 Sociodemographic Characteristics of Respondents

The detailed results of the socio-demographic variables of respondents in this study have been presented elsewhere [14]. The mean age of the respondents was 11 ± 1.93 years, and their ages were classified into the 5- 10 and 11-15 age ranges.

3.2 Knowledge of Schistosomiasis Infection/

Table 2 Shows that a good number (60.8%) of the respondents were aware of schistosomiasis, with about half of them (49.6%) getting information about the infection from family and friends. Only three (0.6%) of them knew that schistosomiasis can be contracted from infected water, while almost all of them didn't consider living close to the river (99.4%) and open defectaion (100.0%) as risk factors for the infection. Very few (12.1%) of them know that blood in urine and feaces are signs of having the infection. Most of them (87.3%) have not seen bloody urine, and the majority (83.9%) of them

Table 2. Respondents' Knowledge of Schistosomiasis

Knowledge questions	Yes (%)	No (%)
Have you heard of schistosomiasis	304 (60.8)	200 (29.7)
before?		
What is the source of your infor-		
mation	10 (2.0)	
Radio	14 (2.8)	
Television	25 (5.0)	
Health workers	250 (49.6)	
Family/Friends	5 (1.0)	
School	200 (39.6)	
Not heard Risk factors of Schistosomiasis		
Contact with contaminated water	2 (0.6)	501 (00.4)
	3 (0.6)	501 (99.4)
Sharing of cutleries with an infected person	0 (0.0)	100 (100.0)
Contact with other's faeces	2 (0.4)	502 (99.6)
Not wearing shoes within the neigh-	0 (0.0)	100 (100.0)
borhood	0 (0.0)	100 (100.0)
Exposing oneself to mosquitoes	1 (0.2)	503 (99.8)
Open defecation	0 (0.0)	504 (100.0)
Living close to a river/stream	3 (0.6)	501 (99.4)
Can schistosomiasis be transmitted	5(1.0)	499 (99.0)
from person to person?	0(110)	.,, (,,,,,)
Symptoms of schistosomiasis in-		
clude:		
Blood in urine/faeces	61 (12.1)	443 (87.9)
Abdominal pain	0(0.0)	100 (100.0)
Body pain	1 (0.2)	503 (99.8)
Frequent urination	4 (0.8)	500 (99.2)
Stunted growth in children	1 (0.2)	503 (99.8)
Skin rash	1 (0.2)	503 (99.8)
Blood from the nose/eyes/ears	1 (0.2)	503 (99.8)
Poor vision	1 (0.2)	503 (99.8)
Have you ever seen bloody urine	64 (12.7)	440 (87.3)
If yes, what do you think was re-	* (-= . ,)	(0,10)
sponsible?		
Spiritual problem	24 (4.8)	
Puberty	7 (1.4)	
Infection	49 (9.7)	
Pile	1 (0.2)	
No idea	423 (83.9)	
Have you received any health talk	30 (6.0)	474 (94.0)
on schistosomiasis before?		
Categorized knowledge		
Good (7.3%)		
Poor (92.7%)		

don't have an idea of what is responsible for bloody urine. Almost all (94%) respondents have yet to receive health talk about schistosomiasis. Although a good number (59.5%) reported being screened for schistosomiasis, very few (7.3%) reported being positive for the infection. A larger percentage (93%) of the respondents had poor knowledge of the infection.

3.3 Respondents' Previous Medical History with regards to Schistosomiasis

Out of the five hundred and four students recruited into this study, a good number (59.5%) reported having been screened for schistosomiasis in their respective schools, and few (7.3%) reported being positive for the infection during school screening (Table 3).

Table 3. Self-reported Previous Medical History of Respondents

Have you ever been diagnosed with schistosomiasis before?		
Yes No What was the outcome of your diagnosis?	300 (59.5) 204 (40.5)	
Positive Negative	22 (7.3) 278(92.7)	

3.4 Respondents' Hygiene Practices Relating to Schistosomiasis Transmission

The results of hygiene practices of respondents with respect to schistosomiasis transmission are presented in Table 4. About a quarter (27.8%) of the respondents use tap water for their drinking water, a little above a third (37.5%) use boreholes for their drinking water, very few (0.6%) drink from rainwater while some of them, though, very few (4.0%) drink river and stream water. With regards to toilet facilities, although a larger percentage (56.5%) of the respondents use a water closet system at home, a few of them (7.5%) still engage in open defecation, while some (4.4%) of them use public latrines. Most (75.2%) of the respondents use only water and soap to clean their toilet, while only very few (9.9%) use water, soap, and disinfectant for their toilet cleaning. Almost (96%) all the students reported having toilet facility within their school premises. Concerning their visitation to the river, about a fifth (21.2%) reported they never visited a river, almost a third (27.4%) visited within the past few days of collecting this data, about a quarter (26.6%), visited within the past few months while about another quarter (24.8%) visited within the past few years. Among those who visit the river, about a fifth (22.6%) reported having defecated or urinated in the river at one time or another. A little below average (43.5%) of the respondents reported fetching water from rivers/streams. The overall practice was categorized as good and poor, with above average (65.1%) of the respondents exhibiting good practice.

3.5 Factors associated with respondent's poor hygiene practices

Tables 5 and Table 6 present the results of the association between selected variables and hygiene practices of respondents related to schistosomiasis using both chisquare and logistic regression models. At the bivariate level, sex, class of respondents, having received health talk, history of previous infection, and their knowledge were statically associated with their practices (P<0.05).

Table 4. Respondents' Hygiene Practices Relating to Schistosomiasis Transmission

Transmission	
Practices	Frequency (%)
Drinking water source Public tap water Borehole Well River/stream Rain	140 (27.8) 189 (37.5) 152 (30.2) 20 (4.0) 3 (0.6)
Domestic water source Public tap water Borehole Well River/stream Type of toilet facility at home	95 (18.8) 161 (31.9) 220 (43.7) 28 (5.6)
Water closet Traditional latrine Public latrine Open defecation in the bush Materials for cleaning toilet	285 (56.5) 159 (31.5) 22 (4.4) 38 (7.5)
None Only water Water and soap Water, soap and disinfectant Availability of toilet facility within school premises Yes	23 (4.6) 52 (10.3) 379 (75.2) 50 (9.9) 484 (96.0)
No Washing hands before and after eating Yes No Washing hands After leaving the toilet	20 (4.0) 404 (80.2) 100 (19.8)
Yes No Washing hands After returning from an outing Yes No Washing hands After touching baby feaces, vomi-	298 (59.1) 206 (40.9) 72 (14.3) 432 (85.7)
tus, urine, etc Yes No Washing hands at regular intervals	215 (42.7) 289 (57.3)
Yes No Last time you visited a river Never Some days ago	100 (19.8) 404 (80.2) 107 (21.2) 138 (27.4)
Some months ago Some years ago How often do you go to the river Never Almost every day	134 (26.6) 125 (24.8) 90 (17.9) 67 (13.3)
A few times a week A few times a month A few times a year Ever defecated/ urinated in or near a river/stream	115 (22.8) 87 (17.3) 145 (28.8)
Yes No Fetching water at the riverside Yes No	114 (22.6) 390 (77.4) 219 (43.5) 285 (56.5)
Swimming Yes No Irrigation farming Yes	181 (35.9%) 323 (64.1%) 270 (53.6%)
No Fishing Yes No	234 (46.4%) 115 (22.8%) 389 (77.2%)
Categorized Practice Good Practice: Poor Practice:	328 (65.1%) 176 (34.9%)

After adjusting for confounders, logistic regression revealed that male respondents were 1.6 times more likely to have poor practices than their female counterparts (aOR 1.6, 95% CI 0.413-0.913), primary four pupils were 1.3 times more likely than their counterpart (aOR 1.3, 95% CI 0.491-3.255), those who have received health talk on the infection were 27 times less likely to have poor practices (aOR 0.37, 95% CI 0.175-0.761), those who reported being positive for the infection were 4.4 times more likely to have poor practice (aOR 4.4, 95% CI 1.703-11.260) and those who had poor knowledge of the infection were 6.0 times more like to have poor practices relating to the infection (aOR 6.0, 95% CI 0.014-0.278).

4.0 DISCUSSION

This study revealed that factors such as sex, having received health talk about schistosomiasis, previous history of schistosomiasis infection, and knowledge of the infection all play a significant role in various hygiene practices that contribute to schistosomiasis infection transmission. Male children in this study being at 1.6-fold risk of poor hygiene practices relating to schistosomiasis is not unprecedented as male children are known for more stream water-related occupational exposure and other water-related activities such as swimming and fishing, a claim supported by other authors [15–18]. Other studies [19,20] have reported sex differences in hygiene practices, with females being more hygienic than males, and this has been attributed to the fact that males tend to exhibit a nonchalant attitude towards hygiene issues compared to their female counterparts. Other researchers have associated some sociocultural beliefs with the sex differences in hygiene practices; for instance, females are not expected to have open baths in rivers like their male counterparts due to some religious or cultural beliefs [17,21].

This study also revealed that respondents' lack of knowledge of schistosomiasis influenced their various practices, which contribute to schistosomiasis transmission. This is not unprecedented as those with good knowledge of risk factors and transmission pathways of schistosomiasis may be well informed about the dangers of unhygienic practices such as river water contact, especially for occupational and recreational activities. Water's role in transmitting Schistosoma infections is well established as the parasite fulfills part of its lifecycle in water habitats harbouring the intermediate snail hosts [22–24].

Table 5. Factors associated with Respondents' Hygiene practices

Variables	D		P-value
Variables	Practices	D	P-value
A	Good	Poor	
Age	1.46 (60.0)	06 (07.1)	
5-10	146 (62.9)	86 (37.1)	
11-16	182 (66.9)	90 (33.1)	0.399
Sex			
Male	154 (59.5)	105 (40.5)	
Female	174 (71.0)	71 (29.0)	*0.007
Father's occupa-			
tion			
Risky	61 (61.0)	39 (39.0)	
Not Risky	267 (66.1)	137 (33.9)	0.350
Mother's occupa-			
tion	28 (63.6)	16 (36.4)	
Risky	300 (65.2)	160 (34.8)	0.869
Not Risky			
Respondent's class			
Primary 2	20 (71.4)	8 (28.6)	
Primary 3	52 (52.5)	47 (47.5)	
Primary 4	99 (68.8)	45 (31.3)	
Primary 5	88 (72.1)	34 (27.9)	
Primary 6	69 (62.2)	42 (37.8)	*0.025
Received health			
talk	20 (51.3)	19 (48.7)	
Yes	308 (66.2)	157 (33.8)	*0.046
No	()		
Previous infection			
Positive	7 (31.8)	15 (68.2)	
Negative	321 (66.6)	161 (33.4)	*0.001
Knowledge	(00.0)	- 31 (55)	0.001
Good	35 (94.6)	2 (5.4)	
Poor	293 (62.7)	174 (37.3)	*<0.00
*	==== (0=)	-7.(57.5)	1

Table 6. Predictive factors of Poor hygiene practices using logistic regression

Covariates	P-value	aOR (95% CI)
Sex		
Male	*0.016	1.6 (0.413-0.913)
Female [ref]		
Respondent's class		
Primary 2 [ref]		
Primary 3	0.627	1.5 (0.283-0.908)
Primary 4	*0.022	1.3 (0.491-3.255)
Primary 5	0.305	1.3 (0.769-2.313)
Primary 6	0.096	1.6 (0.917-2.890)
Received health talk		
Yes	*0.007	0.37 (0.175-0.761)
No [ref]		,
Previous infection		
Positive	*0.002	4.4 (1.703-11.260)
Negative [ref]		(,
Categorized		
Knowledge		
Good [ref]	<*0.001	6.0 (0.014-0.278)
Poor		•

aOR = Adjusted odd ratio, CI = Confidence interval

Thus, whoever has acquired sufficient knowledge on schistosomiasis transmission would take cognisance of the adverse effects of having contact with river water, knowing fully well the role of fresh water in the sustenance of the intermediate snail host of the schistosome parasite. The number of children involved in the practice of polluting water bodies with either feaces or urine in this study is unacceptably high. This may be connected with a lack of sound public health education on the subject matter. It's expected that a good knowledge of schistosomiasis transmission would have prevented the children from such unhygienic practices of polluting water bodies with feces and urine. Even though a good number of respondents in this study were aware of schistosomiasis, only very few had good knowledge of it. This means their awareness does not translate into good knowledge of the subject. This study is similar to a study carried out to assess knowledge attitudes and practices of primary school children about schistosomiasis in Zimbabwe [11], where 32.0% of the children had correct knowledge about the causes of schistosomiasis. In comparison, 22.1% knew correct measures to control the infection. This study is, however, in contrast with a study carried out in Uganda [25] to assess knowledge, attitudes, and practices regarding schistosomiasis infection and prevention, where a total of 98.5%, 81.3%, and 78.5% had heard about schistosomiasis and knew the main transmission modes and symptoms respectively. The good knowledge recorded in the study was attributed to countrywide health education campaigns organized by the Ministry of Health between 2017 and 2018. The impact of such health education is also reiterated in this current study as those respondents who have received health talk on schistosomiasis were reported to be less likely to have poor practices relating to schistosomiasis. Lack of adequate knowledge of the subject among the respondents is therefore reflected in their responses such that only three of them knew that schistosomiasis can be contacted from infected water and almost all of them didn't know that living close to river and engaging in open defeacation can be risk factors of the infection.

This study also revealed that previous history of schistosomiasis infection is statistically predictive of poor hygiene practices. This study observes that most respondents who reported previous infections had poor hygiene practices. This indicates that poor hygiene practices may be a predictor of infection. Although it is expected that those with a previous history of schistosomiasis should have improved their sanitary habits, the reverse is the case in this study. However, this may be a pointer to the fact that infection in this group of children may be triggered due to usual unhygienic practices. Thus, interventions targeting the control of schistosomiasis must put public health enlightenment programs in place to achieve a change in behaviors.

This study revealed that primary school children have poor knowledge of schistosomiasis, which is associated with unhygienic practices that are known to be associated with schistosomiasis transmission. Therefore, behavioral change communication through effective public health education and enlightenment is essential in preventing and controlling schistosomiasis within the State.

Conflicts of Interest

The authors declare that there is no conflict of interests.

Authors' Contributions

TB conceived and designed the study, contributed to data collection, data analysis tools and manuscript writing. OS, AF contributed to data analysis tools. MR, KF contributed to manuscript writing. AO contributed to study design and manuscript writing. MA contributed to study design, data analysis tools and performed analysis of data. All authors approved the final copy of the manuscript.

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