Is Knowledge Power or a Predictor? Assessing Parental Education Associations with *Schistosoma haematobium* infection in Kano State, Nigeria

By

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Abstract

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Background: There are about 250 million people infected with schistosomiasis worldwide—with approximately 300,000 people dying annually. Urogenital schistosomiasis (*S.haematobium*) infects school-aged children at an alarming rate and there is a need to evaluate community-based factors' associations with the infection. This study aims to compare infection levels across levels of parental education in Hausa communities of Kano State, Nigeria.

Methods: The data is a part of the cross-sectional study 'Kano Schistosomiasis in SAC 2019', taken from participants residing in Hausa communities in five local government areas in Kano State. Urine samples were collected and the presence of *S.haematobium* eggs were examined utilizing urine filtration. Tests for association were conducted and a multivariate logistic regression model was used to predict the presence of urogenital schistosomiasis with a focus on sociodemographic predictors such as parental education.

Results: Of the 272 participants, the overall prevalence of urogenital schistosomiasis was 36.9%. The mean age of the study sample was 11 years (4.08 SD). There were 218 (81.34%) males and 50 (18.66) females. The highest caseload was amongst the 12-18-year-old group (45.6%). Out of the infected study sample, mid-range (secondary and technical) parental education had the highest rate of infection (45.9%) compared to low-range (no education to primary level) education and high-range (professional and university) education (35.6% and 18.4% respectively). Questionnaire data revealed 64.3% (173) reported engaging in activities with unprotected water sources, 40.9% (110) did not have knowledge on transmission, and 14.5% (39) reported having a past "worm" disease. The multivariate logistic regression analysis revealed that medium level of education (aOR = 1.29, 95% CI: 0.610-2.74), and low-level education (aOR= 2.22, 95% CI: 0.96-5.11) showed a positive, however, not a statistically significant association with schistosomiasis across ranges when compared to the highest education level.

Discussion: The study shows a high prevalence of urogenital schistosomiasis in children in Hausa communities within Kano State, Nigeria. Although there was not a significant association found between parental education and infection, the lowest range of education showed a positive odds ratio with the presence of *S.haematobium* eggs. This suggests further studies are needed using a larger sample size to better study potential associations.

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CHAPTER 1: INTRODUCTION AND BACKGROUND

Schistosomiasis, also known as bilharzia, is a waterborne parasitic disease that has impacted the lives of hundreds of millions in the developing world causing severe morbidity and mortality. With conservative estimates, there are approximately 250 million affected worldwide, majority within sub-Saharan Africa (Hotez, Fenwick, & Kjetland, 2009). The global burden is estimated to be 2.6 million disability-adjusted life years (DALYs) (Colley, Bustinduy, Secor, and King (2014). To add to its devastating impact, approximately 300,000 people die annually from this disease (Hotez et al., 2009). Despite the complexity of schistosomiasis in respect to its lifecycle and transmission, there is a simple and relatively inexpensive course of treatment. Praziquantel is an anti-parasitic medication widely used to treat schistosomiasis following the standard dosage of 40 mg/kg in one oral dosage (for *S. haematobium* and *S. mansoni*). Studies conducted by the Carter Center showed that Nigeria is the most endemic country for schistosomiasis, even after years of strenuous control efforts. There are approximately 30 million people in the country in need of treatment, with school-aged children being the most vulnerable population. Regarding risk distribution, low risk is considered to be less or equal to 1% to less than 10% prevalence, medium risk is considered to be greater or equal to 10% to less than 50%, and high risk is considered to be greater or equal to 50% (Bishop, 2017). It is crucial to support MDA programmatic worker and healthcare providers in developing countries with the most appropriate tools in order to achieve fast and early diagnosis and treatment of the patient.

The common species of schistosomiasis present in sub-Saharan Africa are *S.haematobium* and *S.mansoni*. *S.haematobium* also known as, urogenital schistosomiasis, affects the urinary and reproductive tracts within a body system (Shebel, Elsayes, Atta, Elguindy, & El-Diasty, 2012). *S.mansoni,* a type of intestinal schistosomiasis, affects the hepatic and gastrointestinal systems (Nour, 2010). Nigeria, in which this research was carried out, is a country endemic for co-infections with both *S.mansoni* and *S.haematobium*. However, urogenital schistosomiasis infects the most people, not only in Nigeria but across the globe (Le & Hsieh, 2017). Due to the complexity of diagnosis, the standard-of-care is not adequate in detecting many infections, especially those of lower worm burden (Utzinger, Becker, van Lieshout, van Dam, & Knopp, 2015). This is especially true for settings that lack adequate laboratory facilities. Due to this, the actual parasitic disease burden is typically higher than detected. To combat this issue there has been a growing body of work on developing sufficient diagnostics, especially for mass drug administration programs (MDA) (Literature Review). The need for sensitive diagnostics is on the rise, for the efficiency of treatment and future vaccines to be accurately measured. In countries such as Nigeria, little is known about the efficacy of molecular diagnostics. This is particularly true amongst school-aged children, who make up 80% of the urogenital schistosomiasis cases in Nigeria (Watts, 2006). More information regarding practical diagnostic tools is needed for programmatic workers and health care providers in developing countries to best implement control/elimination strategies of schistosomiasis.

School-aged children are the standard population in which this disease is studied, due to their large number of infections and the accessibility within schools and health clinics (Poggensee et al., 2005). In the past, researchers and programmatic workers have surveyed areas by diagnosing primarily through hematuria (blood in urine). However, this approach misses asymptomatic as well as low-intensity infections. In studying prevalence, therefore, it is important to have a highly sensitive (detecting true positive cases) and highly specific (detecting true negative cases) diagnostic test. There are many expensive technologies for the diagnosis of schistosomiasis and other parasitic diseases. This leads to inaccessible diagnoses due to the pricing, need for training, and non-portable equipment. Assessing laboratory methods in diagnosing an endemic population will allow those pushing towards control and elimination to greater understand differences within technologies and their strengths and limitations.

Previous studies have focused on the relationship between schistosomiasis and factors such as nutritional status, geographical location, and housing (Atalabi, Lawal, & Akinluyi, 2016; Forson, Arthur, & Ayeh-Kumi, 2018). It is important to study the external factors such as familial influence on the presence of the disease. Education has been used in many studies to represent socioeconomic status. A study done in 2019 showed with each additional year of maternal education, children have a 10% lower probability of dying in Malawi; while in Uganda the odds of dying for children of women with one additional year of education are 16.6% lower (Andriano & Monden, 2019). This study aims to explore risk levels of schistosomiasis across different parental education levels as well as assess the current diagnostic capacity in the field of schistosomiasis. This is in order to develop and sustain impactful interventions where there is a focused target profile described by risk factors and accurate diagnostics. Several diagnostics tools that have potential to be field deployable, were compared in order to aid programmatic workers within MDAs and healthcare workers to form an accurate prognosis in a low resource setting. In addition, several demographic, clinical experience with worm infections, and water usage variables were collected and assessed for secondary analyses.

CHAPTER 2: LITERATURE REVIEW

The Lifecycle of Schistosomiasis/Bilharzia

Schistosomiasis is a parasitic disease caused by the trematode flukes of the genus Schistosoma. There are five species known to infect humans: *Schistosoma haematobium, Schistosoma mansoni, Schistosoma japonicum, Schistosoma intercalatum, Schistosoma mekongi*—each distinguished by egg morphology. The lifecycle of the parasites is a very interesting and complex one. It involves two hosts: snails and mammals. Snails are the natural reservoirs where asexual reproduction occurs, and mammals are the host for sexual reproduction (Lardans & Dissous, 1998). Asexual reproduction occurs in freshwater snails, specifically for Nigeria, in *Bulinus* and *Biomphalaria* species for *S.haematobium* and *S.mansoni* respectively. Miracidium hatch out of eggs from urine or feces in freshwater. They search the water to find a specific snail species to infect and within snails, the development of miracidia into sporocysts occur. Sporocysts multiply and grow into the infectious form of the parasite, the cercariae. Cercariae are released out of the snail host at a 1:1000 miracidia to cercariae ratio (Nelwan, 2019). Humans contract the disease when they come in contact with contaminated water through activities such as fetching water, washing clothes or swimming (Colley et al., 2014). The cercariae get the opportunity to enter through skin, secreting proteolytic enzymes that widen the skin pores (Shebel et al., 2012). They then shed their forked tail and become schistosomula (Nelwan, 2019). Schistosomula grow into schistosomes and adult worms, existing in various locations within the body.

Regarding urogenital schistosomiasis, *S.haematobium* migrates through the bloodstream to the bladder, ureters, and possibly rectal venules. Once in the mammalian host, parasites mature after six to eight weeks. Once matured, females start producing eggs, up to 300 per day (Adebayo et al., 2017). The eggs are deposited in the small venules of the porta and perivesical systems. Depending on the species they can progress to the lumen of the intestine (*S.mansoni, S. japonicum, S.mekongi, S. intercalatum*) or the bladder and ureters (*S. haematobium*). *S. haematobium* is the sole cause of urinary schistosomiasis, and is responsible for two-thirds of the disease cases globally (Noriode, Idowu, Otubanjo, & Mafe, 2018). Some eggs become trapped in the organ systems and cause damage resulting in the devastating outcomes of intestinal and urogenital schistosomiasis. Others diffuse through the wall of the organ system and exit the body through defecation or urination, contaminating the water source and beginning transmission again (Colley et al., 2014). A well-developed, adult version of this species is cylindrical and elongated in shape. The egg possesses a terminal spine, which can cause morbidity and granulomatous lesions due to the host immune response. Therefore, the WHO International Agency for Research on Cancer has declared *S.haematobium* a group 1 carcinogen (Awosolu, Shariman, Haziqah, & Olusi, 2020).

History of Diagnosing Schistosomiasis

There has been a variety of methods employed to accurately diagnose positivity of schistosomiasis and level of infection. The selection of methods relies on the conditions of diagnosis, including the resources available, type of sample, and the environment deployed. In a clinical setting of a non-endemic area, a detailed history is taken, including but not limited to a patients' origin, recent travels, and contact with rivers, lakes, or streams. However, because a clinical picture of schistosomiases is nonspecific laboratory tests are required. Microscopic analysis of stool or urine serve as the traditional diagnosis for both intestinal and urogenital schistosomiasis, despite limitations. The main technique is Kato-Katz (KK), which has great applicability in determining intensity of the infection. This technique involves detecting the presence of eggs in stool or urine. Although this test is considered the standard-of-care, it is not very sensitive, meaning it misses many true infections—especially in a low transmission/worm burden areas (He et al., 2016).

Molecular Detection Methods

In recent decades, there has been a boom in research and development of drugs as well as diagnostics in the field of NTDs. Diagnosis of schistosomiasis is crucial for accurate mapping and surveillance of controlled/post-elimination areas. In 2012 there was a push for highly sensitive and specific diagnostics tools, especially adaptable to low transmission areas (Utzinger et al., 2015). There has been ongoing research for developing alternatives for standard diagnostics such as antibody-based detection of circulating cathodic antigen (CCA), circulating anodic antigen (CAA), Polymerase Chain Reaction (PCR)/DNA-based methods, mobile microscopy, and microfiltration technology (Le & Hsieh, 2017). CCA and CAA utilizes lateral flow (LF) assays to diagnosis the antigen of the parasite. A study showed CAA detecting an active infection in 56 out of 81 exposed individuals (69%) (van Grootveld et al., 2018). Another study demonstrated successful use of recombinant CCA, without false-negative results as well as providing high sensitivity and specificity. However, there has been criticism of its inconsistent sensitivity; showing results similar to the KK smear and inadequacy at detecting *S. haematobium* (Lodh et al., 2017). DNA detection has become gradually popular amongst the diagnostic field for its high specificity and sensitivity. For PCR, the DNA is first extracted from the sample and purified. Afterwards, it goes through cycles of heating and reheating in order to amplify the DNA of the parasite—until it reaches a threshold of detection. Although more sensitive than classical methods, such as the KK method, its high purchasing costs and extraction requirement serves as barriers for making it the gold standard. Loop-Mediated Isothermal Amplification (LAMP) is another novel method studied and tested by researchers. Similar to PCR it can amplify and detect DNA from human samples. Alternatively, this method does not entail the use of expensive equipment, however, it still requires an extraction step and can lead to false positives (Weerakoon, Gordon, McManus, & disease, 2018). Other diagnostics methods such as Single Molecule Sequencing (SMS), that use gene sequences, have been put forward but require more validation through research studies and require more training of practitioners (He et al., 2016).

Treating Schistosomiasis

Praziquantel, an anti-helminthic drug, is a non-toxic drug that is highly effective at treating schistosomiasis at a low cost. Thanks to organizations like the Gates Foundation, WHO, and the United States of Agency for International Development (USAID), generic medications and drug donation programs have been made available to the masses in many affected countries for as a little as $0.32 per solution (Hotez et al., 2009). The recommended single oral dose, 40 mg/kg, results in more than a 95% reduction in egg excretion (Touré et al., 2008). A study done in Egypt showed that the consequences of urogenital schistosomiasis such as hematuria, bladder cancer, and kidney damage can be avoided with regular issued praziquantel treatment starting at a school-age level (Fenwick, 2006).

However, there are still flaws within the therapeutic system of schistosomiasis. Through more sensitive diagnostics, it has been proven that anti-Schistosoma therapy with praziquantel is only partially effective at reducing the worm burden of active infection. In other words, MDA alone is not sufficient in curing. Currently, there is no present recommendation for 'intensive disease management' (IDM) for older/post-infection illnesses or a 'preschool-friendly' formulation of praziquantel for infants-toddlers to avoid growth impairment (King, 2017). In order to overcome some pitfalls in treatment for the next decade, there has been objectives laid out to optimize praziquantel treatment. Objectives include completion of Phase III trials and licensing of a pediatric formulation, new drug and vaccine development, and complex trials integrating drug, snail control, behavior change, and WaSH interventions (King & Dangerfield-Cha, 2008).

Snail control strategy

Schistosomiasis is caused by parasitic worms that require snail hosts to complete its lifecycle. Due to this, snail control strategies are considered a priority for the reduction of schistosomiasis transmission. Existing control methods are aimed mainly at the management of snail populations that inhabit known endemic areas. One of the most popular forms for killing snail populations susceptible to worm invasion is using chemicals in environmental water sources. A study done by (Lo et al., 2018) modeled transmission of schistosomiasis and cost effectiveness of various strategies in low- and high-prevalence rural Kenyan communities. They simulated strategies over a 10-year period of MDA targeting, snail control, and combined strategies. The results supported inclusion of snail control to the global guidelines and control strategies for optimal control, seen in over 95% of simulations.

In areas affected by irrigation development, sufficient drainage and environmental engineering have been effective in reducing both *S. haematobium* and *S.japonicum* transmission (Lardans & Dissous, 1998). Specifically, the use of molluscicides such as niclosamide and molluscicdal plants historically function as a supportive procedure. However, a downside to these methods is the toxicity that threatens fish and surrounding environments. Therefore, alternative methods have been developed to combat chemical downfalls. In the past the introduction of snail competitors that are resistant to schistosomes has been considered in order to compete for parasites by possible decoy effect (Combes & Moné, 1987). Unfortunately there is a potential for the new snails to become susceptible to the local schistosome, as seen in a study done in Brazil (Lardans & Dissous, 1998).

History of Schistosomiasis in Nigeria

The first reported case of bilharzia was not until 1908, 57 years after Theodor Bilharz first described the parasitic infection. It was not until 1922 when physical deterioration and other debilitating symptoms were associated with the disease (Farley, 2003). Nigeria is in a unique position, containing a variety of risk factors that contribute to the massive morbidity and mortality experienced by its citizens. The health problems are linked to inadequate water supply, poverty, lack of sanitation services and impoverished housing conditions. Its growing population remains vulnerable to the schistosomiasis. Although schistosomiasis is one of the most common NTDs throughout the world, Nigeria has the greatest number of cases worldwide with about 29 million infected and 101 million people at risk of infection (Dawaki et al., 2015). It is estimated that this disease forfeits approximately 70 million disability-adjusted life years (DALYs) every year. Children of ages between 0-14 years make up 43.01% of the population structure (Bishop, 2017).

Schistosomiasis can affect all populations but has the worst impact on children, especially those who indulge in water-contact activities (like swimming, wadding, etc.). Most studies describe preschool-aged children (PSAC) as under 4 years old and school-aged children (SAC) between 4-18 years old. In a study of 251 school-aged children in two communities of Ovia South West LGA of Edo State, Nigeria (Noriode et al., 2018) the prevalence of urinary schistosomiasis was 65.3%. The authors noted that the results "indicate increasing transmission when compared with a rate of 8.1% that was reported by the national survey conducted in 2012." They associated the high prevalence in the study areas to the "general unavailability" of a consistent safe water supply and sufficient sanitary facilities within communities. Another study by Yauba (Yauba et al., 2018) found 238 out of 385 (62.0%) children displaced by Boko Haram to have urinary schistosomiasis in Maiduguri, Nigeria.

More relevant to this study, (DAWAKI et al., 2016) looked at Hausa communities in Kano State, Nigeria. They conducted a cross-sectional study among 551 participants aged 1-90 and found an overall prevalence of schistosomiasis to be 17.8%. The lower prevalence can be explained by the inclusion of an older population. Adults who practice unprotected irrigation farming, fishing, or domestic chore-related activities from cercariae-infested water bodies are also prone to schistosomiasis. A good portion of the Nigerian population is mostly unaware of these risks, leading to greater rates of transmission and increased incidence.

Socio-determinants/Risk Factors of Infection

Several factors influence the risk for schistosome infection within the population. The association between poverty, poor sanitation and the infection has been demonstrated across Africa in many studies (Nyati-Jokomo & Chimbari, 2017) (DAWAKI et al., 2016). However, there are additional factors that can increase the probability of contracting the infection. In her literature review regarding the social determinants, Watts found that the infection was disproportionately affecting the poor and female (Watts, 2006). This is due to women having more roles that involve water contact compared to men; including washing, laundry, and carrying household water. She examined children of school age (see above) and found a significant link between the infection and stunting of growth. In a cross-sectional study of 620 participants, there was a direct link to a dependency on the river and contracting an infection. Being within the 10-14-year-old range also played a role, as the group had the highest prevalence of 65.9% (Awosolu et al., 2020). Data from studies based in Nigeria (Atalabi et al., 2016), 2016), (Ogbonna et al., 2012), and (Amuta & Houmsou, 2014), 2014) showed a significant association between children that reported activity with farming and irrigation and the infection. Interestingly so, the Atalabi study also identified an association between the mother's occupation and presence of infection, specifically the brown collar jobs (cooks, maids) and housewives. (Atalabi et al., 2016).

Parental Education Associations with Schistosomiasis

The associations between education, poor sanitation and infection with schistosomiasis have been demonstrated across Africa as well as many other socio-determinants discussed above. Particularly education has been linked to children health outcomes, primarily because of the link between education and nutrition. A study containing 376,992 participants across 56 countries showed nutritional returns to parental education generally increased but were highly variable across country sub-samples (Alderman & Headey, 2017). Another study, done in Ghana, took a random sample of 300 children aged 2-9 years used structured pre-tested questionnaire and stool tests to analyze these associations. It showed that children from mothers and fathers with no education were often infected (62.2% and 55.6% respectively) however the educational status was not significant at p=1.0 (Forson et al., 2018). In a study of 168 parent informants in northwestern Tanzania, 48.3% parents had misconceptions about the cause, modes of transmission and control of schistosomiasis (Angelo et al., 2019). This demonstrates gaps within the knowledge of schistosomiasis amongst adults and uncertainty regarding associations between parental education and children's disease status. This ambiguity in the literature justifies further exploration of this association. The study of interest aims to narrow the existing gap.

CHAPTER 3: METHODS

Study Design

Data from the study, "Kano Schistosomiasis in School-Aged Children 2019" were used to conduct this study, collected between June 2019 to July 2019. The overall design of this study was cross-sectional in order to collect data from school-age children and guardians as well as diagnose the infection by the current standard-of-care (microscopy) in real time. This was conducted among patients ranging from ages 4-18 years in both high and transmission areas. The different transmission areas were targeted in order to evaluate the efficiency of molecular diagnostics in detecting different levels of intensity in future studies. Parents and guardians of children positively diagnosed by the standard-of-care were referred for treatment. Local community health facilities were also given information about their respective prevalence. Samples from health facilities and in-field collection came from 5 Local Government Areas (LGAs) in Kano State, Nigeria. The selected districts were Kura (8.429°E and 11.774°N), Bebeji (8.400°E and 12.366°N), Gwarzo (7.932°E and 11.915°N), Minjibir (8.530°E and 12.226°N), and Kano Municipal (11.9600° N, 8.5007° E). Kano Municipal is the low prevalence area while the rest are moderate to high prevalence areas. The climate of the study area was tropical dry-and-wet type, and the study took place during wet season (May-October). Participants were randomly selected in both a health facility setting and school setting. In health facilities, every 3rd person was chosen for the study. In school settings, every other child was chosen to participate in the study.

Collection occurred between the optimal time of 10am and 2pm into 50 mL clean containers with wide mouth and screw-cap. The samples were properly labeled with the respective study ID # (Location#-Research assistant #-Daily participant #). The samples were transported within 5 hours of collection in suitable cool bags at temperature between 4 and 6 C for subsequent examination at the International Foundation Against Infectious Disease in Nigeria (IFAIN) at eHealth Africa. A total of 300 children amongst 5 health facilities and 2 schools participated in the study by responding to a questionnaire and providing the required urine sample.

Study Population

This study was conducted in Kano State, Nigeria a metropolis of almost 11 million people. The age range was selected due to the variability of disease in children compared to adults. Children remain at a higher risk of infection due to their less matured immune systems. The study area is largely inhabited by Hausa-speaking people.

Procedures

Prior to enrollment into this study, a comprehensive site-specific protocol and multiple standard-of-procedures were developed for training local research assistants. The individuals who agreed voluntarily to participate in the study had their urine documented, filtered and viewed under a microscope for standard-of-care diagnosis with signed written consent. Then individuals were interviewed using a structured questionnaire. Participants were interviewed face-to-face in health and school facilities by at least one research assistant trained with the purpose of administering questionnaires.

Urine samples were examined by direct microscopy, urine filtration, and iodine staining methods for the presence of *S. haematobium* eggs (Fig. 2).To determine worm burden, the egg count was taken and recorded as eggs per 10 milliliters of urine (EP10mL) for each sample. The intensity of infections was also recorded as light (1-50 EP10mL) and high (> 50 EP10mL) (DAWAKI et al., 2016). For quality control, 30% of the samples were re-examined for the presence of the Schistosoma eggs by at least one other parasitologist.

Questionnaire

Structured questionnaires designed to elicit information on water contact, previous diagnoses, experience with MDA programs, and other control activities in the communities were used to collect data from the school children. In addition, community health care providers were administered questionnaires to assess their knowledge, awareness, and perceptions of the disease as well as their experiences with diagnosis and treatment. The questionnaires for the children were aimed to gather demographic information (such as the independent factor for analysis, parental education) while that of health care providers probed into their knowledge of how the disease affects their community, measures for preventing infection and challenges that impede control/elimination efforts.

Data Management/Statistical Analyses

Data were double entered by two different researchers on a notebook and subsequently on spreadsheets in Microsoft Excel. Then a third researcher crosschecked the data sets for accuracy and created a single data set for analysis. Demographic, socioeconomic, environmental and behavioral characteristics were treated as categorical variables and presented as frequencies and percentages. All statistical analyses were preformed using SAS 9.4. Descriptive statistics were used to calculate the prevalence and intensity of urogenital schistosomiasis. The Pearson Chi-square test was used to assess the associations. A multivariate logistical regression was conducted across the following paternal education levels: university/professional, secondary, technical/vocational. University/Professional was defined as the highest level of education, secondary was equivalent to a high school/GED education, and technical/vocational was defined as a school primarily for practical skills, controlling for age and sex.

Ethical Consideration/Approval

Full approval was given by the Institutional Review Board of Emory University RSPH before the commencement of the study under the following protocol: IRB00111157. In addition, approval was obtained from the local ethical board, the Ministry of Health in Kano State, the respective local government authorities, and the district heads. Written and signed consent forms were obtained directly from the participant if they were 18 years. Written and signed consent forms were directly obtained from the guardian and assent from the participant if they were between 6-17 in the study. These procedures were also approved by the ethics committees.

CHAPTER 4: RESULTS

The socio-demographic characteristics of the respondents are presented in Table 1. Although there were 272 children enrolled in the study, only 268 participants had their questionnaire information recorded. Out of this number, 218 (81.34 %) males and 50 (18.66 %) females. There were 23 (8.55 %), 110 (40.89%), and 136 (50.56%) participants in the age group, 0-5, 6-11, 12-18 respectively, with a mean age of 11 years and a standard deviation of 4.08.

Table 1. Socio-demographics characteristics of school children examined in Minjibir, Gwarzo, Kura, Bebeji and Kano Municipal local governing areas n= 268

Variables	Frequency	Percentage (%)
Sex		
Male	218	81.34
Female	50	18.66
Age		
0-5	23	8.55
6-11	110	40.89
12-18	136	50.56
Education Level of Participants		
Primary	127	61.65
Secondary	79	38.35
Unanswered	60	22.56
School System of Participant, % (n)		
Islamic	49	18.22
Western	19	7.06
Both	191	71.00
None	8	2.97
Occupation of Guardian		
Full-time Student	14	6.34
Agriculture	166	61.94
Public Sector	10	3.73
Teacher	20	7.46
Private Sector	19	7.09
Domestic	14	5.02
Other	16	5.97
Unemployed	12	4.48
Locations		
Bebeji	64	23.52
Gwarzo	37	13.60
Kura	38	13.97
Kura Primary School	45	16.54

Minijibir	51	18.75
Kano Municipal	37	13.60

n= actual number of subjects

Prevalence

In the study, 272 school-aged children had their urine samples collected and examined for the presence of *S. haematobium* with 100 children found to be infected by *S.haematobium* as shown in Table 1. The overall prevalence was 36.9% amongst the locations used for this study in Kano State, Nigeria. The highest prevalence (60.5%) was recorded among children in Kura's major hospital, compared to Bebeji, Gwarzo, Kura, Kura Primary School, Minijibir, Kano Municipal with prevalence rates of 21.8%, 45.9%, 57.8%, 23.5%, and 13.5% respectively (see Table 2).

Table 2 shows the prevalence of infection by age range and sex. The highest prevalence was among the age group 12-18 (45.6%) and the lowest among the age group 0-5 (8.7%) as shown in Fig.3 (P=0.001). The infection rate was higher among males (37.6%) than females (34.0%) but was not statistically significant (P=0.633). Out of the 100 positive children, 69 (69.0%) had light intensities of infection with egg counts of <50 eggs/10 ml of urine while 31 (31.0%) had heavy intensities of infection with eggs of more or equal to 50 eggs/10ml of urine. The age group 6-11 had the highest percentage of heavy infections (47.7%) compared to age groups 0-5 and 12-18 which were 0% and 24.2% respectively but was not statistically significant (p= 0.134) as shown in Table 3.

Table. 2 Prevalence by Location, Age Ranges, and Gender				
Variables	Total		X^2	P-value
	Examined	Infected (n,%)		
Locations			**23.33**	**0.0003**
Bebeji	64	14 (21.8)		
Gwarzo	37	17 (45.9)		
Kura	38	23 (60.5)		
Kura Primary School	45	26 (57.8)		
Minijibir	51	12 (23.5)		
Kano Municipal	37	5 (13.5)		
Total	272	100 (36.9)		
Age Ranges			**13.50**	**0.001**
0-5	23	2 (8.7)		
6-11	110	35 (31.8)		
12-18	136	62 (45.6)		
Gender			**0.23**	**0.633**
Male	218	82 (37.5)		
Female	50	17 (34.0)		

*prevalence out of 272 due to 3 missing containers

Table. 3 Level of Intensity amongst infected school-aged children in Kano State, Nigeria				
Variables	Number infected (Prevalence, %)		X	P-value
	Light intensity	Heavy intensity		
Total	69 (69)	31 (31)		
Age Ranges			**4.01**	**0.134**
0-5	2 (100%)	0(0%)		
6-11	19 (54.3)	16 (47.7)		
12-18	47 (75.8)	15 (24.2)		
Gender			**0.01**	**0.916**
Male	57 (69.5)	25 (30.5)		
Female	44 (88.0)	6 (12.0)		

Associations Amongst Different Parental Education Levels and Infection

Among the children positive for *S.haematobium* ova, children of parents with a low-level education had a higher rate of infection (47.0%) than children of parents with mid-level and high-level education whose rates were 37.7% and 34.8% respectively. The status of education levels of parents using high-level education as a reference were as followed: Technical (aOR= 1.784, 95% CI 0.618-5.149), Secondary (aOR= 1.107, 95% CI 0.506-2.422), Primary (aOR= 3.362, 95% CI 1.192-9.486), None (aOR=0.946, 95% CI 0.435-2.056). Varying levels of education did not represent a statistically significant risk of infection for the children (Table 4).

Table. 4 Multi-Logistic Regression of varying levels of Parental Education with Presence of Infection among school-aged children in Kano State, Nigeria

Education Levels	**Infected (n,%)**	**Not infected (n,%)**	**Total**	**Multivariate**	
				cOR 95%CI	aOR 95%Cl*
High-Level	16 (34.8)	30 (65.2)	46	Reference	-
Mid-level	40 (37.7)	66 (62.3)	106	1.136 (0.552-2.341)	1.293 (0.610-2.740)
Low-level	31 (47.0)	35 (53.0)	66	1.661 (0.765-3.607)	2.218 (0.962-5.114)
Overall	99	170	218*	-	-

*adjusted for age range and gender

*excluding “other”, “refused”, “don’t know” responses

**p-value related to AOR; overall refers to overall model

*** University as a reference

Risk Factors Associated with Urogenital Schistosomiasis

Bore-holes, wells, rivers, public fountains, rainwater, and tanker trucks were indicated as sources of water for domestic use. Out of 269 respondents, 173 (64.3%) said they had previously engaged in activities with unprotected water sources. Table 5 lists out the different unprotected sources of water the participants identified. Unprotected wells were the top source of unprotected sources, with 105 (60.7%) participants engaging in activities linked to it. The activities that were identified within and around water bodies include playing, swimming, fetching of water, laundry/washing of clothes and fishing. Participants were also asked questions around their knowledge of urogenital schistosomiasis. Regarding knowledge of risk factors for transmission, 39 (22.2%) reported drinking contaminated water, 75 (42.6%) reported bathing, 20 (11.4%) reported fetching contaminated water, 2 (1.1%) eating unwashed food such as fruits and produce, 6 (3.4%) reported fishing in infected water, 9 (5.1%) poor hygiene/sanitation habits, 1 (0.57) reported sexual contact, 10 (5.7%) reported urinating in contaminated places, and 23 (13.07%) reported did not know how the infection is transmitted. In the sample size of 269 participants, 39 reported knowledge of a previous diagnosis of a worm-related disease. Amongst the children positive for *S.haematobium,* 20 (20%) reported to have been previously diagnosed with a parasitic disease while 79 (79%) were not.

Table 5. Frequency of Risk Factors and Knowledge Associated with Urogenital Schistosomiasis in Kano State, Nigeria

Variables	Frequency*	Percentage (%)
Unprotected sources of water for drinking, cooking, washing, bathing		
Public Fountain	5	2.89
Unprotected Well	105	60.69
River	42	24.28
Rainwater	21	12.14
Knowledge on Transmission**		
Yes	23	13.29
Don't Know	110	63.58
Knowledge of Risk Factors for Transmission***		
Drinking	39	22.16
Bathing	75	42.61
Fetching	20	11.36
Unwashed Food	2	1.14
Fishing	6	3.41
Hygiene	9	5.11
Sex	1	0.57
Urinates	10	5.68
Don't Know	23	13.07
Previous Diagnosis		
Yes	39	14.50
No	230	85.50
Previous Knowledge of Schistosomiasis		
Yes	118	43.87
No	151	56.13
Previous Usage of PZQ		
Yes	224	82.65
No	47	17.35

*96 respondents either unanswered or answered "don't know"
**missing 136 responses
*missing 93 responses

CHAPTER 5: DISCUSSION/CONCLUSIONS

This cross-sectional study showed active schistosomiasis to be a common infection in school-aged children from 4-18 years old in the selected LGAs. The burden of urogenital schistosomiasis in the area (36.9%) falls within the WHO classification as moderate prevalence (between 10% to 50%). This prevalence was observed amongst the 5 LGAs (Minjibir, Gwarzo, Kura, Bebeji and Kano Municipal). The prevalence reported in Kura proved to have the highest rate (60.5%) compared to the other study sites, while the lowest was seen in Kano Municipal (13.5%) an urbanized area in Kano. The prevalence is in accordance with prevalence rates reported by previous studies; 44.2% Minjibir LGA of Kano State (Duwa, Oyeyi, & Bassey, 2009), 50.3% in Kadawa and Kano State (Bassey & Umar, 2004), and 42.7% in 44 LGAs of Kano State (Abdullahi (Abdullahi, Bassey, & Oyeyi, 2009). However, the prevalence in this study contrasts to those reported in other LGAs of Kano State such as 17.8% Dawaki's study (DAWAKI et al., 2016). The present study revealed there to be no significant differences in infection rates across parental education. However, the study did show that the odds of having urogenital schistosomiasis are about 2.2 times higher for a child of parents with no education to primary level education compared to a patient with university level education, controlling for age and sex. The results of (Forson et al., 2018) showed similar outcomes in their study, who found a positive odds ratio between education levels of both mothers and fathers and schistosomiasis (OR = 0.9779, p = 1.0) and fathers (OR = 1.845, p = 0.0719). They used a similar sample size in their study (n=300), which further suggests addition studies needed with larger sample sizes to demonstrate the association.

Males were reported to be more infected than females; this could be due to the higher tendencies of water contact activities among males like swimming, playing and laundry which exposes both sexes to infection. Similar findings were reported by Kanwai and Dawaki. They found males to be more infected than females in Igabi, Kura, Bebeji, Gwarzo, Shanono and Minjibir LGA of Kaduna State and Kano State, Nigeria (Kanwai, Ndams, Kogi, Gyem, & Hena, 2011) (DAWAKI et al., 2016).

The age-related prevalence showed that children aged 12-18 years had the highest prevalence. This trend has also been reported in several previous studies which attributed factors like swimming, washing, fishing, and playing in infested water bodies to the high prevalence in the age group (Noriode et al., 2018) (Nyati-Jokomo & Chimbari, 2017). These various activities have also been reported among children examined in this study. However, children aged 6-11 had the highest rates of heavy infections (47.7%) compared to 0-5 and 12-18 age groups, 0% and 24.2% respectively. This could be attributed to the fact that there was a primary school included in the study population, skewing the results. There was a low infection rate amongst the 0-5 age group. This is in discordance with the study conducted in Guma LGA of Benue State, Nigeria which found a considerably high rate infected (44.9%) in the area (Amuta & Houmsou, 2014).

With regard to the knowledge, attitudes, and perceptions towards schistosomiasis, especially urogenital schistosomiasis; over three quarters (85.5%) did not have a prior parasitic infection while 56.1% reported no previous knowledge of schistosomiasis, referred to as *Tsargiya* in Hausa. This could be attributed to a lack of intervention efficacy within communities (Ross et al., 2017). Of the 269 respondents, 96 reported using sources of water that were covered/protected. The study revealed that the majority of the respondents used unprotected sources for drinking, cooking, washing and/or bathing (64.3%). Approximately 61% those who reported using unprotected sources, indicated unprotected wells to be there primary source of water. This could be due to the lack of political will of a subset of the stakeholders to finalize some of the pipe-borne water projects seen in some communities. The lack of this resource drives inhabitants to completely rely on streams and public fountains, increasing their risk of infection through exposure. Further investigation into experiences of schistosomiasis revealed that a majority of participants had previously taken PZQ (82.6%).

It may be assumed that the reported prevalence of schistosomiasis was underestimated of the true prevalence in the study population due to the financial, methodological and temporal limitations inherent in carrying out this cross-sectional study. However, it is important to note the high prevalence amongst the study sample given the limited diagnostic means. In the study population, approximately 37% of all participants were positive for active infection—presenting *S.haematobium* eggs in their urine. This research adds to a growing body of literature exposing North Nigeria's high infection rate compared to other parts of the country. The high prevalence and intensity of infection in the study areas are strongly associated with the general unavailability of a safe water supply and adequate sanitary facilities in communities and the reliance of unprotected sources like river bodies and wells (Angelo et al., 2019). Dependence on these sources for water supply poses an unavoidable risk of multiple infections for inhabitants.

There were several limitations implicit in both the methodology and diagnostic techniques that undeniably affected study results and possibly contributed to an underestimation of the prevalence. Although there was an effort made by the researcher to design a study that could utilize the standard-of-care detection techniques in resource-limited settings, train and work cooperatively with local staff and make treatment accessible to study sites; there is a high probability of error within one or more steps.

Regarding the use of syringe urine filtration as the standard-of-care when diagnosing urogenital schistosomiasis, numerous researchers have criticized this method (Le & Hsieh, 2017) as well as the probable underreporting by missing light infections (Gray, Ross, Li, & McManus, 2011). Urine samples should be ideally collected and tested over three days (Bassey & Umar, 2004) however, there were a number of samples that had to be evaluated over 4 days after collection. There were also certain samples that needed to be discarded due to an inadequate amount of urine, lack of consent/assent, or lack of an additional factor.

The questionnaires were useful at identifying demographic variables and prior schistosomiasis exposure as well as data for the independent variable of interest, parents' education. However, using questionnaires brings in recall bias as participants have to remember information from months to years ago. In addition, although 269 school-aged children that provided answers to questionnaires, there were some questions that were left unanswered possibly skewing the results.

In conclusion, the prevalence levels observed in this study show that the communities require an integrated control approach that includes on-going mass chemotherapy. The lack of resources regarding sanitation and water supply has led to the adoption of unsafe water practices. Awareness of disease among the school-aged children within this study was very poor; a subset of them believed that the blood in their urine was associated maturity. Many respondents did not have prior knowledge of the disease. There is a need for education on parasitic diseases to be incorporated into school curriculums widely through North Nigeria. Due to the lack of sensitive and accurate diagnostics, we expect the results to be an underestimation. There will be a follow up study using highly sensitive methods discussed in the Literature Review.

CHAPTER 6: PUBLIC IMPLICATIONS/RECOMMENDATIONS

This study shows there is a clear significant prevalence of urogenital schistosomiasis in Kano State, Nigeria. This situation is present among school-aged children up until the age of 18. There appears to be a relationship between parental education and the presence of *S.haematobium* eggs in school-aged children. As education decreased, the odds of infection increased. Although this was not statistically significant at a=0.05, it should be noted that the diagnosis was made with the standard-of-care, microscopy, known to miss many cases especially in low intensity cases. Given this fact, the prevalence was still very high (over 1/3 of the sample population). It is expected that with a highly sensitive method (able to accurately detect new, low-burden infections) there would be a higher number of positive cases identified. This finding necessitates sensitive and validated diagnostics to be employed at large, in order to show the true number of cases in a given population. The field of molecular diagnostics, as mentioned previously, is promising for detecting neglected tropical diseases. Methods such as ELISA and LAMP are being used in rapid diagnostic tests (RDTs), which manufacturers are starting to explore developing at scale (Weerakoon et al., 2018). It also emphasizes the need for an increased recognition of urogenital schistosomiasis amongst young children in both urban and peri-urban populations. More studies need to be carried out in these populations with the inclusion of additional components to therapy. The WHO recommends mass drug administration (MDA) with a single oral dose of 40 mg/kg of praziquantel for global control and elimination of the disease. However, this strategy mainly produces short-term benefits such as reduced morbidity. Sustained benefits are debatable given low MDA coverage, low drug compliance and efficacy, and rapid re-infection rates (Ross et al., 2017). Possible interventions to include are educational or infrastructure components as seen in the northern KwaZulu-Natal province, South Africa (Mogeni, Vandormael, Cuadros, Appleton, & Tanser, 2020). They showed that access to piped water significantly reduced the intensity of re-infection among school children. It is also extremely important to consider the social determinants when developing interventions. The complex disease is a result from associations between poverty, poor sanitation, and geographic locations. In a study done in Zimbabwe, participants indicated behavioral patterns within their environment that are known to increase risk of infection (Nyati-Jokomo & Chimbari, 2017). Though testing and treating are essential elements, eliminating Schistosoma parasites will take a holistic approach that spans the environment in which individuals live and interact with water bodies. Considering the social determinants of the infection and behavioral elements can balance out drug administration, testing and vector control when developing a holistic approach to eliminating schistosomiasis by 2025— for the next generation of Nigerians.

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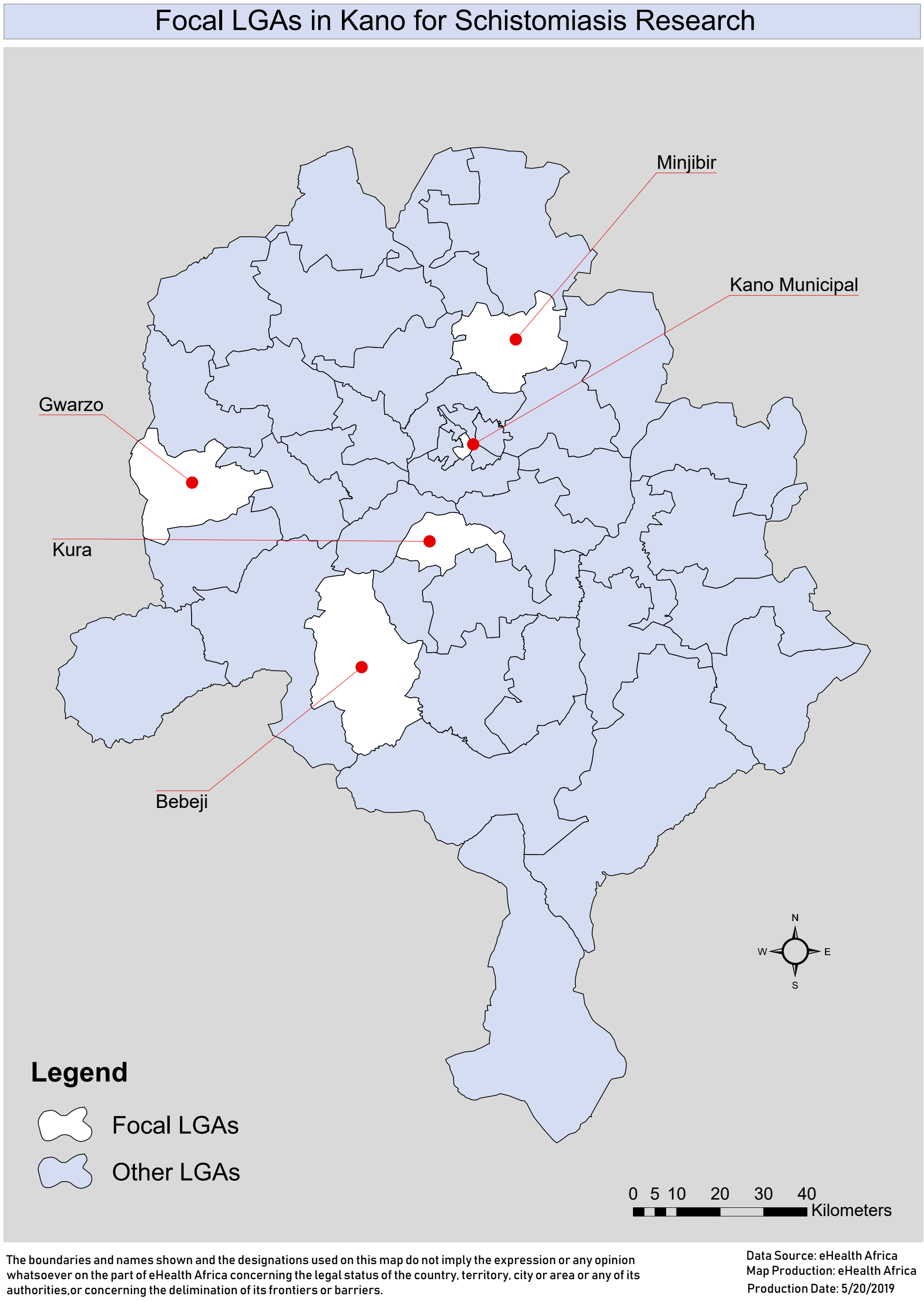

Fig. 1 Focal LGAs in Kano, Nigeria for Schistosomiasis Research

A geographic map showing the location of the districts involved in the study.

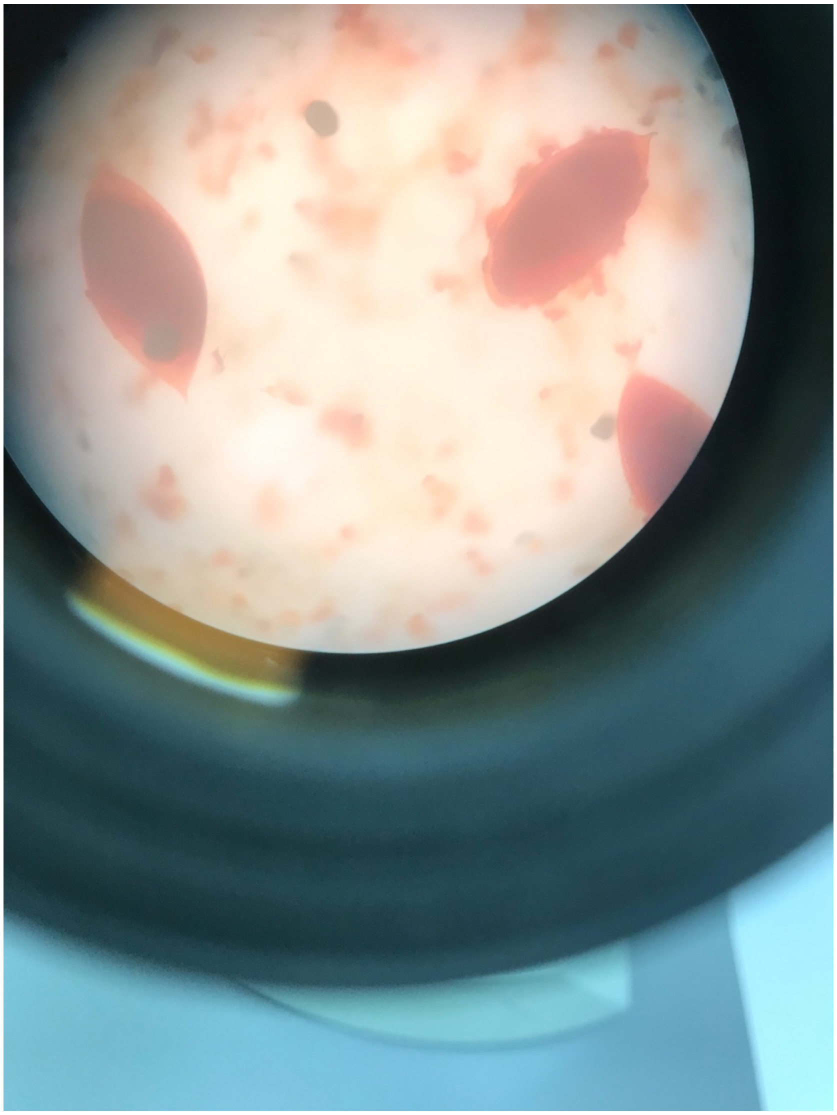

Fig 2. Example of a *S. haematobium* egg