THE EFFICACY OF TREATMENT ON *Schistosoma mansoni, Schistosoma haematobium* AND SOIL TRANSMITTED HELMINTHES AND ITS EFFECTS ON ANTISCHISTOSOME IgE LEVELS AMONG PRIMARY SCHOOL CHILDREN IN TAVETA , KENYA.

By

ISABELL WAIRIMU KINGORI, B.Sc., M.Sc.

I80/91621/2013

A THESIS SUBMITTED TO THE SCHOOL OF BIOLOGICAL SCIENCES, UNIVERSITY OF NAIROBI, IN FULFILLMENT FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN APPLIED PARASITOLOGY

DECEMBER 2017

DECLARATION

This thesis is my original work and has not been presented for a degree in any other university.

Isabell Wairimu Kingori

The University of Nairobi

_____ Date _____

This thesis has been submitted with our approval as university supervisors

Dr. W. T. Mutahi
Supervisor
The University Of Nairobi

_____ Date _____

Dr. Charles Mwandawiro
Supervisor
Kenya Medical Research Institute

_____ Date _____

Professor Dorcas Yole
Supervisor
Technical University of Kenya

_____ Date _____

Dr. Anne Muohi
Supervisor
University Of Nairobi

_____ Date _____

DEDICATION

I dedicate my work to all aspiring PhD students in Kenya and confirm to them this truth "Nothing is impossible with God" Luke 1:37. "What is impossible with men is possible with God" Mathew 18; 27. (Holy Bible, NIV).

AKNOWLEGDEMENT

First and foremost I acknowledge God almighty, the creator of all for giving me the grace and fortitude to successfully accomplish this thesis.

I would like to honor Dr. Mutahi Thuku, my principal supervisor for the crucial role he played in this study. My sincere appreciation goes to Dr. Charles Mwandawiro, who was fundamental in the implementation of this study. Special thanks go out to Dr. Anne Muohi, and Professor Dorcas Yole, who supported, supervised my work, encouraged and guided me accordingly.

My sincere gratitude goes out to all my family and friends who supported me in immeasurable ways during my study. I am grateful to my two children Eva Wambui and Daniel Kingori, who are a blessing from God and with whom we prayed for this PhD to be a reality. They are blessed of the LORD and may they be a blessing to many. I am greatly indebted to Mr. and Mrs. Kingori my parents who supported and encouraged me in immense ways. Sincere appreciation goes out to Cassian Mwatele, Celestine Ufeli, Stella Kulola, Wilson Kingori and Patrick Maina in KEMRI. I thank Esther Kagasi and Collins Kisara in IPR. I also acknowledge the assistance the entire Taveta district hospital team including; Odna, Warfa, Raffael, Mama Njogoro, Morris, Said, Saul, and Mzee Joseph. I also appreciate the help of head teachers, teachers and pupils of; Kiwalwa Primary School, Abori primary school, Eldoro Primary School and Lotima Primary School in Taveta, who played a vital role in providing data for this study. Finally I would like to appreciate Ignatius Weru and Lucy Ngaga from the University of Nairobi, Chiromo Campus.

ABBREVIATIONS

Short Form	Abbreviations
CR	Cure Rate
CDC	Center for Disease Control
DALY	Disability Adjusted Life Years
ESRC	Ethics and Scientific Review Committee
ELISA	Enzyme Linked Immunosorbent Assay
ERR	Egg Reduction Rate
EPO	Eosinophill peroxidase
EPG	Eggs per Gram
FcR	Fragment crystallizable Receptor
IgE IgA, IgG	Immunoglobulin classes
IL	Interleukin
ID	Identification
KEMRI	Kenya Medical Research Institute
L3	Larvae stage 3
OD	Optical Densities
SSC	Scientific Steering Committee
STH	Soil Transmitted Helminthes
SWAP	Soluble worm antigen preparation
SEA	Soluble Egg Antigen
Th	T Helper cell
USA	United States of America
WHO	World Health Organization

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Helminth infections caused by soil-transmitted helminths (STHs) and schistosomes are among the most endemic, communicable diseases of humans who live in parts of the developing world. All-inclusive strategies for the prevention of worm infections; including regular monitoring of infections, regular deworming and environmental sanitation, have significant impact on child health, growth and cognitive development. Monitoring the prevalence of infection and immunological effect of treatment for primary school children with single and dual schistosomiasis infection has been less researched, reported and documented.

This study sought to investigate the infection status of *Schistosoma mansoni*, *Schistosoma haematobium* and soil transmitted helminthes in primary school going children in Taveta Sub-county, Kenya. The study also delved into the infection status of the children after treatment and the significance of treatment on IgE production. This was guided by the prevalence and intensities of the worm infections in the school children before and after treatment.

Data for this study was collected with the assistance of staff from the local health facility, Taveta district hospital and 4 local primary schools in the area. The sampling frame included 442 primary school children of both sexes in the county. Baseline data on the prevalence and intensity of infection, and antibody levels was collected before the yearly national deworming activity in the first year of the study. Follow-up data was collected at 8 weeks and one year after treatment. Stool and urine samples were examined using the Kato- Katz technique and nucleopore filtration methods respectively. Antibody detection and quantification was done by micro ELISA technique by standard operating procedure with slight modifications, after optimization and standardization.

All statistical analyses were conducted in STATA Version 12.0 statistical package. The observed overall prevalence of both *S. mansoni* and *S. haematobium* were calculated by sex and age groups. Confidence intervals of 95% (95% CI) were calculated by binomial logistic regression. Differences in prevalence between the two schistosome species were calculated by the Wald test. Comparison of prevalence by sex and age groups (5-7, 8-10, 11-13 and >13 years old) were tested for significance using the Fisher's exact test. The significance of the factors associated with infection of *S. mansoni* and *S. haematobium* in the school children was determined using the multivariable logistic regression model reporting the odds ratio at 5% significance level and 95% confidence intervals. Factors for the infection were selected using forward step-wise variable selection method. Differences in proportions by age, sex and school were assessed by logistic regression and differences in means using chi-square test, relationships were tested by the correlation co-efficient. Risk ratio was used to calculate the risk of infection in the primary school children. The non parametric Wilcoxon sum rank tests (Mann-Whitney *U* tests) for the independent samples were performed to compare IgE levels against SEA and SWAP in the periods before and after treatment. A quartile regression was performed to check the relationship of the IgE levels with age.

The overall prevalence of *S. mansoni* was 11.8%, (95%CI 8.7%-14.6%) while that of *S. haematobium* was 24.3 %, (95%CI 20.4%- 28.4%) respectively. Further analysis revealed

that out of the 442 primary school children 24 had dual infection (*both S. mansoni and S. haematobium).* Eight weeks after treatment the overall prevalence of *S. mansoni* was 1.13% (SD=0.5%, 95%CI 0.15%-2.12%), while that for *S. haematobium* was 5.58 %(SD=1.5%, 95%CI 2.63%-8.53%) respectively. One year after treatment, the prevalence of *S. haematobium* and *S. mansoni* was 16.9% and 4.28% respectively. Prevalence of infection with *S. mansoni* was significantly reduced for the 13 and above age group in the period of eight weeks and one year after treatment, equally reducing the risk of infection.

STH were not prevalent in the study area, this could be attributed to mass deworming and health and hygiene practices in the study area.

The average overall IgE levels before treatment as measured by optical density decreased from 0.128 to 0.07 after treatment indicating a decrease which suggests a reduction in infection. The IgE levels increased by 0.000875 for every additional increase in the age of the children and the relationship was found to be significant ($P < 0.05$) after the treatment. This study did not find any association between IgE levels and intensity of infection.

This study has generated new knowledge on *Schistosomiasis* and STH infections and the effects of chemotherapy in primary school children in Taveta.

CHAPTER 1

INTRODUCTION AND LITERATURE REVIEW

1.1 Introduction

Schistosome and soil-transmitted helminth (STHs) are parasitic infections that have been classified among the most common infections in developing countries (WHO, 2015). The infectious agents that cause schistosomiasis are hosted by specific freshwater snail vectors. The infectious form of the schistosome parasite is identified as cercariae. It is shed by the snail intermediate host and infests water. Infection occurs through the human skin, when an individual comes in contact with infested freshwater (CDC, 2012). Over history, it has been established that majority of human infections are transmitted by three species of schistosomes: *Schistosoma mansoni, Schistosoma haematobium*, or *Schistosoma japonicum*. In the African continent infections with *S. mansoni* and *S. haematobium* are most prevalent and which are transmitted by host snails of *Biomphalaria* and *Bulinus* genera respectively.

Infection with schistosomiasis is widespread in tropical and sub-tropical areas, especially in underprivileged communities which lack access to safe drinking water and ample sanitation. Worldwide infection with schistosomiasis is estimated at over 240 million people (WHO, 2014). The chemotherapeutic agent of choice that is recommended for all forms of schistosomiasis is Praziquantel. The drug is highly efficacious and safe. Even though re-infection may occur after treatment, the risk of developing severe disease is diminished and even reversed when treatment is initiated and repeated in childhood (WHO, 2015). At least 90% of individuals requiring treatment live in Africa, and 40 million people were treated for schistosomiasis in 2013 (WHO, 2015).

Soil-transmitted helminth infections are cosmopolitan and affect the poorest and most underprivileged peoples. These infections are transmitted through the fecal oral route by eggs

present in human fecal matter which contaminates soil in areas where there is poor sanitation. An exception from this rule is the hookworm that is transmitted through the human skin by individuals walking barefoot. The common helminths that infect people are the common intestinal roundworm (*Ascaris lumbricoides*), whipworm (*Trichuris trichiura*) and hookworms (*Necator americanus* and *Ancylostoma duodenale*) (WHO, 2015).

It is estimated that more than 1.5 billion people or about 24% of the world's population are infected with soil-transmitted helminthes. It is approximated that 270 million preschool-age children and 600 million school-age children live in areas where there is intensive transmission of STH (WHO, 2015). When considered in terms of disability-adjusted life years (DALYs) lost, which translates to the number of healthy years lost to early death or disability, STH infections are as significant as tuberculosis or malaria (Brooker, 2010).

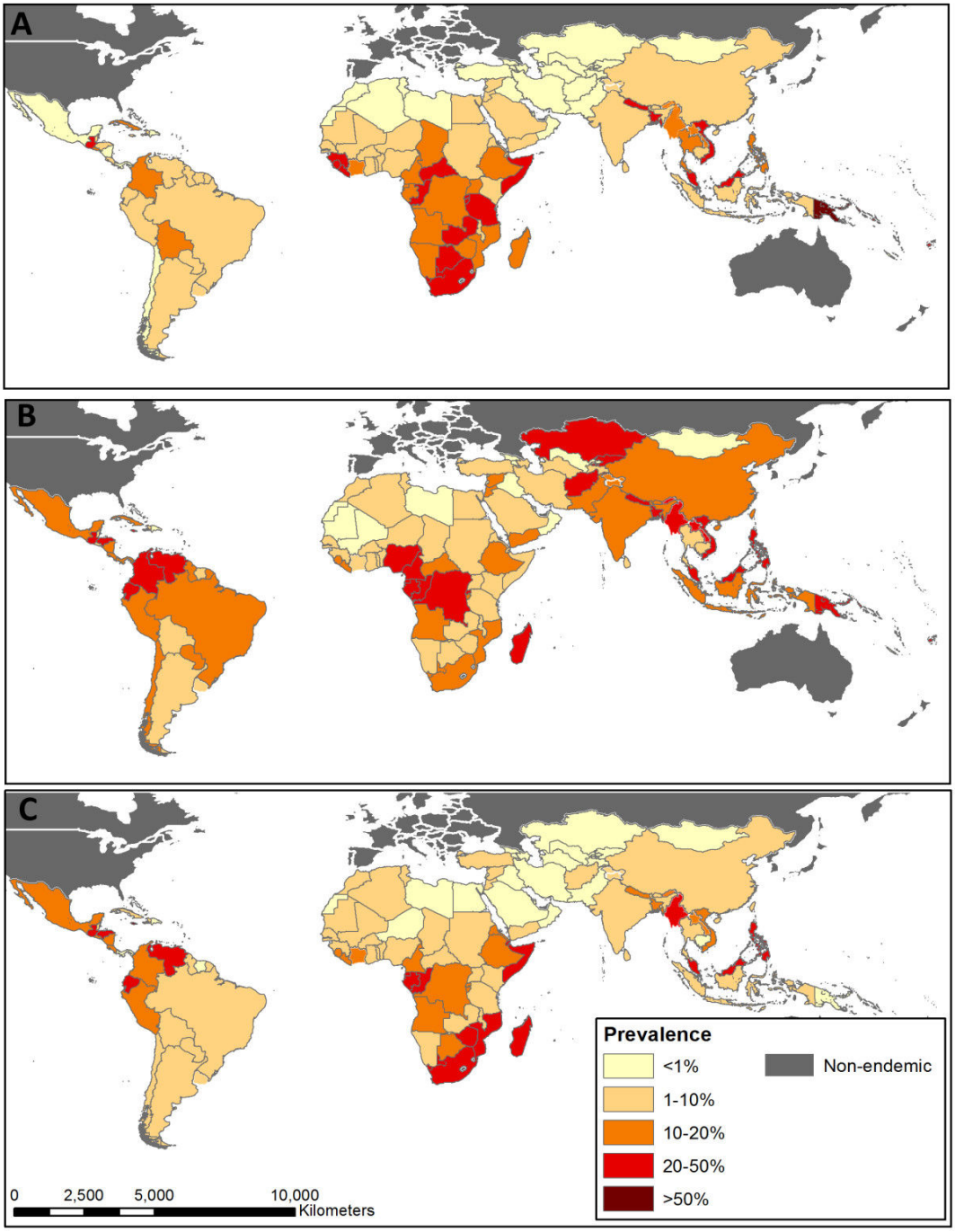
The World Health Organization (WHO) has recommended one of four antihelminthics for the control of STH infections. These are: albendazole, mebendazole, levamisole or pyrantel. It is estimated that the costs for drug administration of STH are US$ 0.012–0.91 per subject (Brooker *et al.*, 2008; Montresor *et al.*, 2010).

1.1.1 Global distribution of STH and schistosomiasis

Global distribution of STH

Soil transmitted helminthes have a global distribution. Figure 1-1 below shows in details STH endemic regions of the world (Rachel *et al.*, 2010). Of the three common STH, *Ascaris lumbricoides* shows extensive distribution. National mean infection prevalence indicates that peak rates of transmission have been observed in the African continent: Cameroon, prevalence of (30.8%; Nigeria (25.4%); Congo (32.2%), and Equatorial Guinea (38.8%). The Asian continent

equally has got high national prevalence rates: Bangladesh (38.4%); Malaysia (41.7%); Afghanistan (36.0%); Philippines (33.6%); Kazakhstan (22.7%); Kyrgyzstan (23.7%); Morocco (8.0%) and Jordan (19.2%). Other countries showing infection with *Ascaris lumbricoides* include: Syria, Arab Republic, Yemen and Palestine. Hookworm infections are common all through sub-Saharan Africa: Eritrea (2.3%); Central African Republic (30.5%); Papua New Guinea (60.6%); Malaysia (21.0%); Nepal (30.7%) and Bangladesh (22.3%). In North Africa the prevalence of hookworm was (6.0%). The prevalence of *Trichuris trichiura* was highest in Malaysia (49.9%), Philippines (45.5%); Central Africa (11.8%); Equatorial Guinea and Central America (38.8%) El Salvador (5.1%) and Venezuela (28.4%). (Rachael *et al.,* 2010)



(A) Hookworm, **(B)** *Ascaris lumbricoides* and **(C)** *Trichuris trichiura*

Figure 1-1: Global Distribution of STH infection prevalence in 2010 by STH species. (Rachael *et al* 2014)

The global distribution of the three common types of STH i.e. hookworm, *Ascaris lumbricoides* and *Trichuris trichiura*. Colored areas indicate the areas where STH are endemic

Global distribution of schistosomiasis

Estimates prevalence and size of endemic regions indicate that the most affected areas are in the African continent as seen in Figure 1-2. These countries include Angola, Central African Republic, Chad, Egypt, Ghana, Madagascar, Malawi, Mozambique, Nigeria, Senegal, Sudan, Tanzania and Zambia. Important prevalence rates have also been observed in Brazil, Philippines, Yemen Arab Republic (Mendis *et al.,* 2007).

With regard to infectious species prevalence *Schistosoma mansoni* is the most prevalent being endemic in 55 countries including the Arab peninsula, Egypt, Sudan, and Libya, Sub-Saharan African countries, Brazil, Some Caribbean islands and Venezuela (Barakat *et al*., 2013) as seen in Figure 1-2.

Schistosoma haematobium is endemic in 53 countries in Africa and the Middle East, where more than 110 million people are infected (Olveda *et al.,* 2013 and Barakat *et al.,* 2013) . *Schistosoma japonicum* is endemic in China, Indonesia and Philippines where about 60 million individuals are at risk of infection. It is approximated that two million individuals are currently infected (Olveda *et al.,* 2013). *Schistosoma japonicum* was eradicated from Japan, the last case of human infection being recorded in 1977 and infected snails were last detected in 1982 (Chistulo *et al.*, 2000).

Schistosoma mekongi is endemic along the Mekong River and some tributaries in the lower Mekong basin. It is approximated that 140,000 people are at risk for infection with 80,000 in Cambodia and a further 60,000 in Laos (Olveda *et al*., 2013). *Schistosoma intercalatum* is prevalent in the rain forest areas of Central Africa (Barakat *et al*., 2013). Two main distinct species have been recognized: one in Zaire and one in Lower Guinea (mainly Cameroon) (Olveda *et al.*, 2013).

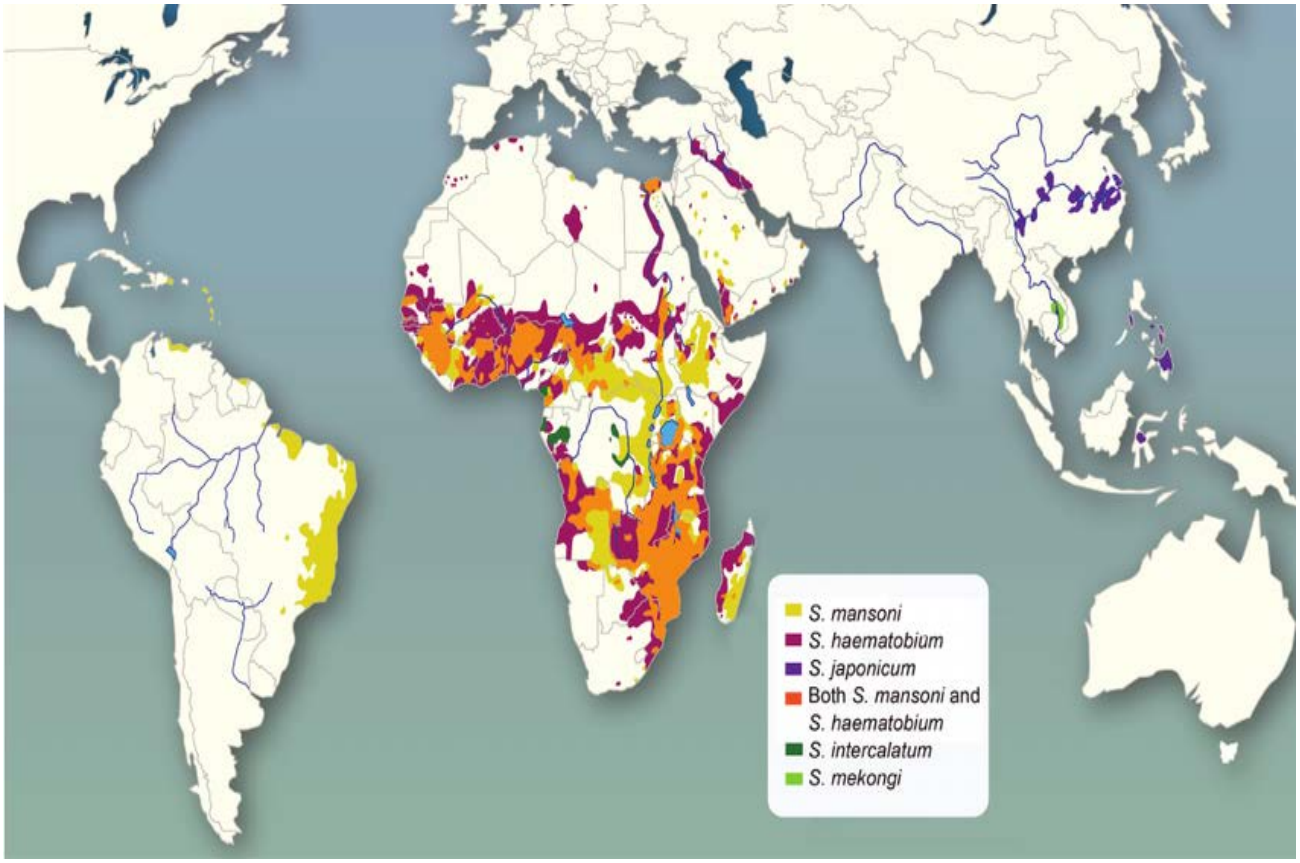


Figure 1-2: Global distribution of schistosomiasis. Source: U.S Center for Disease Prevention and Control (Olveda *et al*., 2013)

The colored areas in the map indicate distribution of *Schistosoma* species globally

1.1.2 Distribution of STH and schistosomiasis in Kenya

Distribution of STH in Kenya

Prevalence of STH in Kenya is mainly distributed in the western and coastal regions as seen in Figure 1-3. A recent study conducted among 199 schools in STH transmission zones in Kenya; demonstrate a national prevalence of 32.3% (Okoyo *et al*., 2016). The prevalence of STH was highest in Western Kenya while pockets of high hookworm prevalence were observed in the coast region.Vihiga county was identified as a hot spot for *Trichuris Trichura* The prevalence of hookworm infections was between 20-50% in Bungoma, Busia, Kakamega, Migori, Kilifi and

Kwale counties. The prevalence of *Ascaris lumbricoides* was between 20-50% in Bomet, Kericho, Kisii, Narok Nyamira, Bungoma, Kakamega and Vihiga counties (Okoyo *et al.,* 2016)..

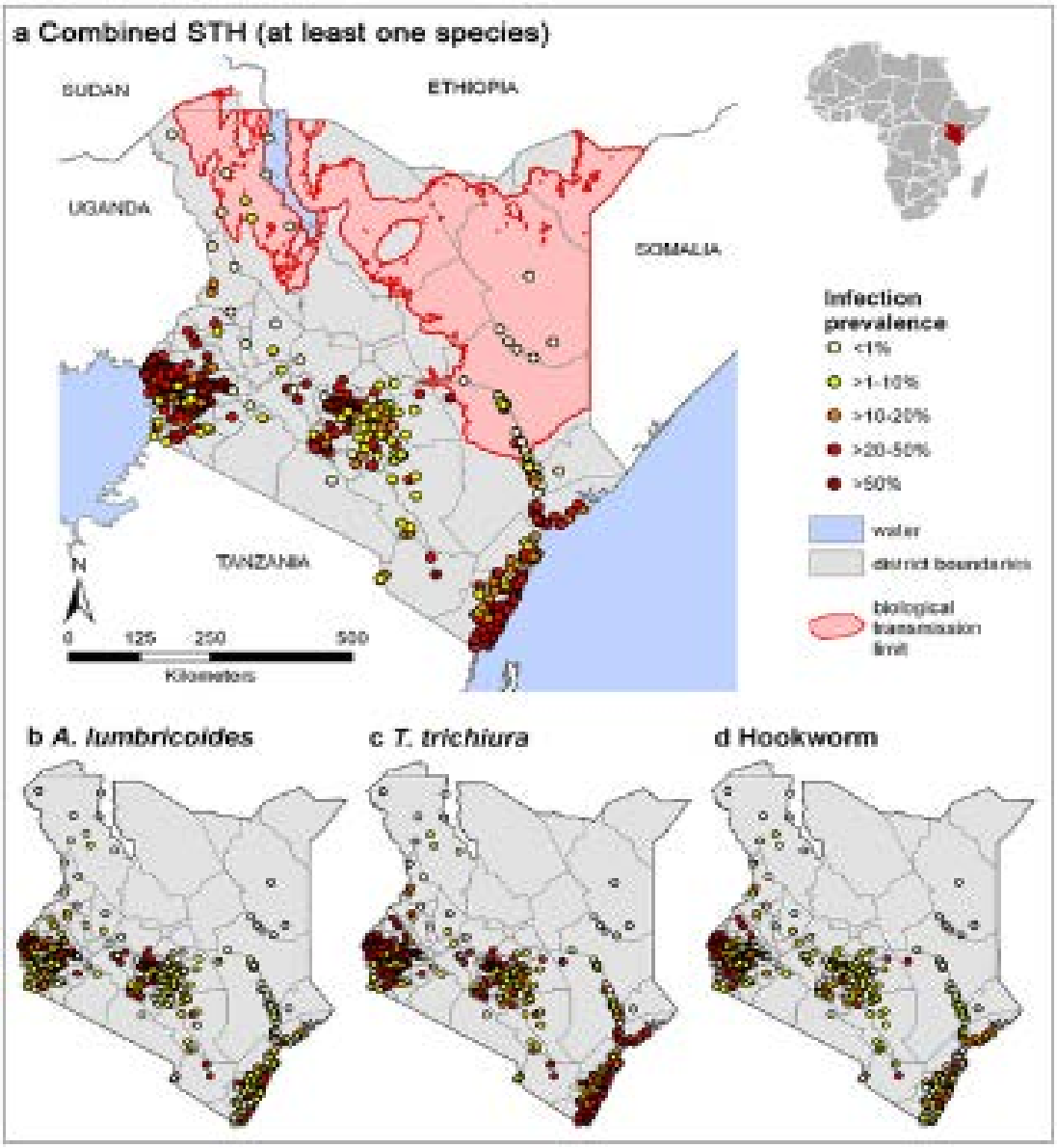


Figure 1-3: Distribution of STH in Kenya (Rachel *et al*., 2014)

The spotted areas in the map indicate the prevalence of STH in different regions in Kenya.

Distribution of schistosomiasis in Kenya

Geographical distribution of Schistosomiasis is associated with water bodies and regions of major occurrence are in central, western and coastal Kenya as shown in Figure 1- 4.

In the western region of Kenya out of 310 children from eight primary schools in Mbita, 238 (76.8%) were infected with *S. mansoni*, while seven (2.3%) were infected *S. haematobium*. (Nagi *et al.,* 2014). Similarly a study of children aged between one to fifteen years conducted in Usoma area in Kisumu County, revealed that overall prevalence of *S. mansoni* for the study population was 39% (Verani *et al.,* 2011).

In the coastal region, a recent survey conducted in Taveta among 470 primary school children revealed 44% infection rate by either *S. mansoni*, *S. haematobium* or co-infection with both species (Gouvras *et al.,* 2013).

In Mwea region of central Kenya a prevalence of *S. mansoni* 53.7% has been recorded (Masaku *et al*., 2015).

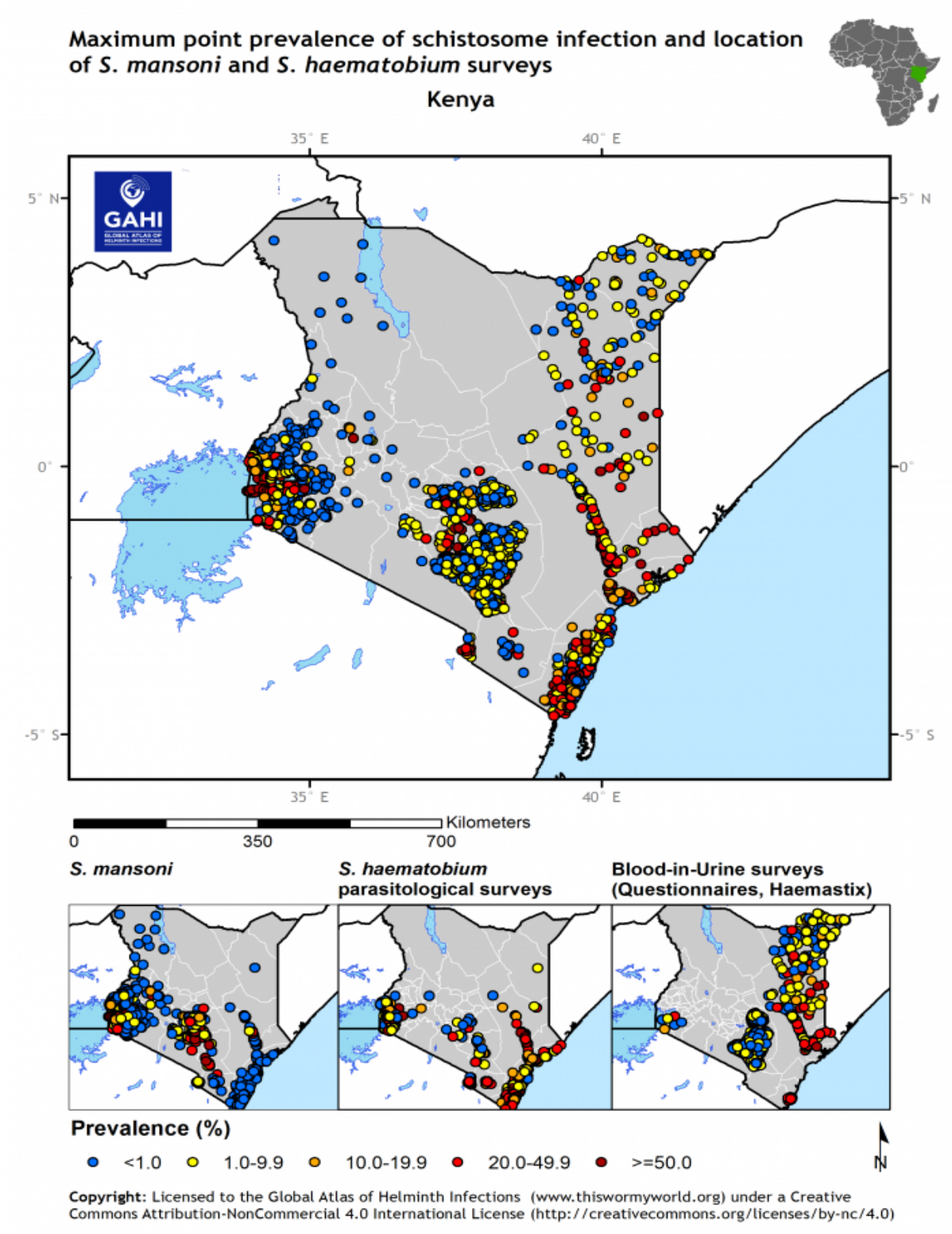


Figure 1-4: Distribution of schistosomiasis in Kenya (Racheal *et al* 2014)

The spotted areas in the map indicate the prevalence of *S. mansoni* and *S. haematobium* in different regions in Kenya.

1.1.3 Life cycle of Soil Transmitted Helminthes

Children get infected with intestinal worm in their daily activities through contact with soil that has been contaminated with human faecal matter from an infected individual. Commonly for *Ascaris* and *Trichuris*, infection occurs when a child ingests the worm eggs, either by eating contaminated fruits or vegetables or by ingesting contaminated soil (WHO, 2012). The eggs are normally passed out in faeces of an infected person. They then undergo embryonation in soil before they become infective, which takes about 8-50 days. For the process of embryonation to occur, certain factors must be appropriate; the soil needs to be loose and moist, it has to be oxygenated, and temperatures must be over 15ºC. It is highly likely that STH eggs survive unfavourable conditions for a long time, and embryonated eggs can easily be carried away from the place of contamination into houses by hands, feet, and shoes or in dust by wind. Once swallowed by a human being the eggs hatch in the intestinal canal. Normally in children the usual vehicle is an unwashed fruit or other food eaten raw. Unwashed hands and children picking up things from the floor or ground and putting them in their mouths, or simply handling contaminated objects like toilet doors etc. are also common ways of acquiring infection as seen in Figure 1-5.

For *Ascaris lumbricoides,* the larvae penetrate the intestinal wall and get to the liver through the portal system. From the liver, the larvae are passed through the right side of the heart and into the lungs. They penetrate the lungs where they undergo two developmental moults to the fourth larvae stage and later pass through the bronchiole, bronchi and trachea to the pharynx. The larvae are swallowed back to the gastro-intestinal tract where they inhabit in the small intestine as seen in Figure 1-6. The larvae mature and start producing eggs in 2 months and can live for about a year (Nordberg, 1999).

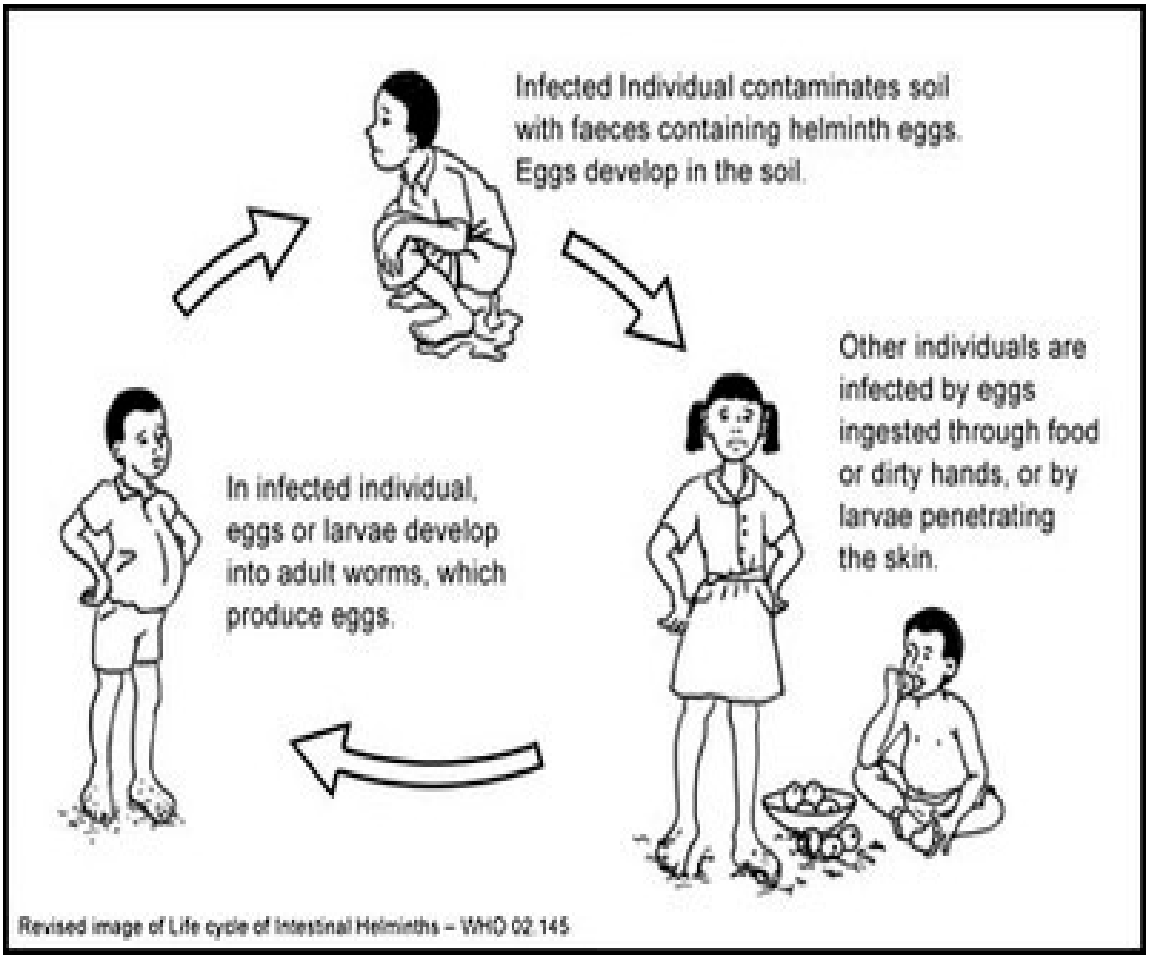


Figure 1-5: General Life cycle of soil Transmitted Helminthes (WHO, 2014)

Infection with *Trichuris trichura* occurs in a similar way to ascariasis. When embryonated eggs are ingested they hatch in the small intestine. The mature worms attach to the mucosa of the caecum and colon (Nordberg, 1999). The only difference with the life cycle in Ascaris lumbricoides is that there is no lung passage for *Trichuris trichura*, as seen in Figure 1-7.

After the eggs of *Trichuris* are ingested, the larvae hatch in the small intestine and penetrate the intestinal villi where they undergo two developmental moults to the fourth stage larvae. They later move to the large intestine where they penetrate the mucosa and develop into adults. Mature adults, start producing eggs (Nordberg, 1999).

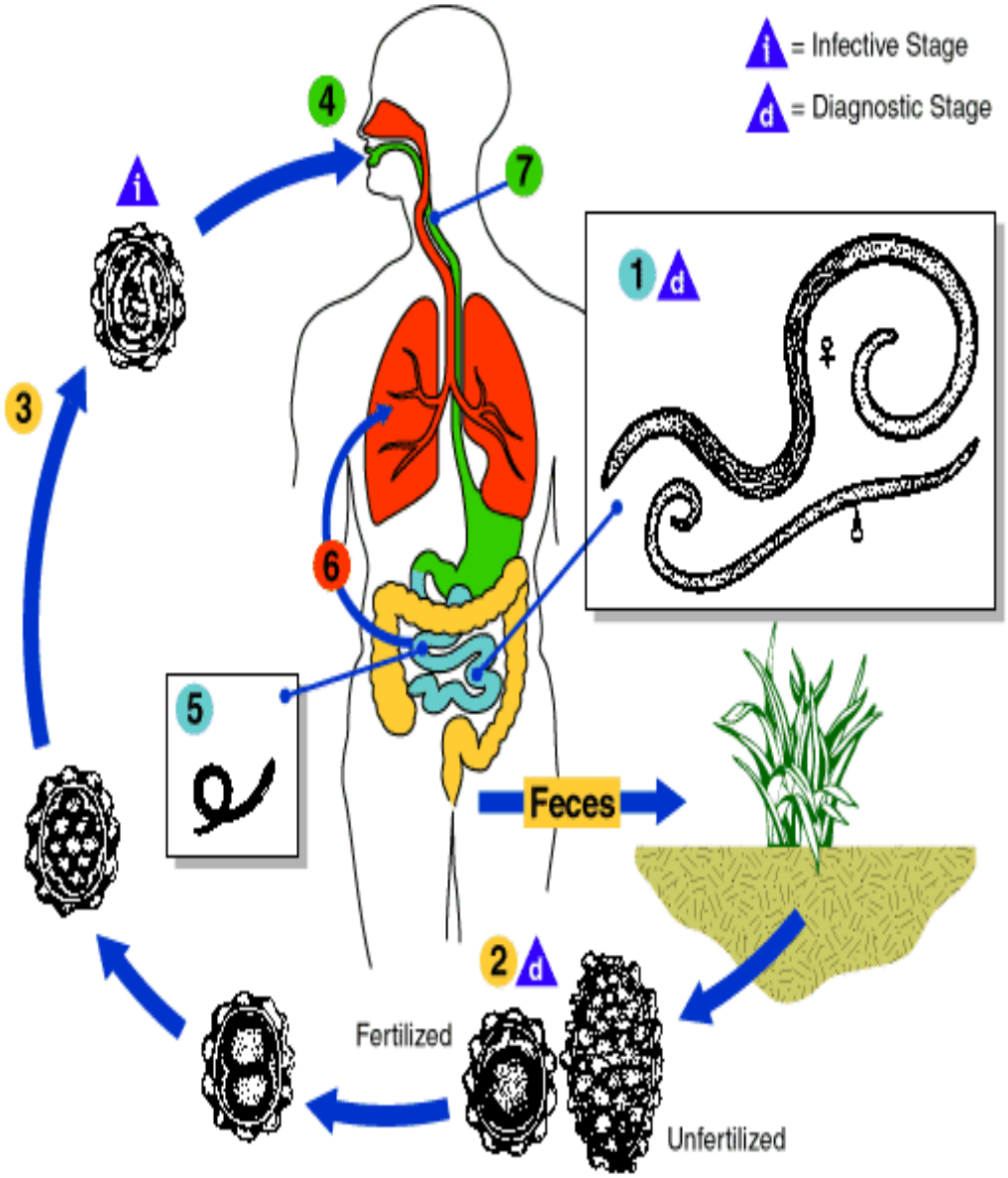


Figure 1-6: Life cycle of *Ascaris lumbricoides*

(https://msu.edu/course/zol/316/alumgut.htm)

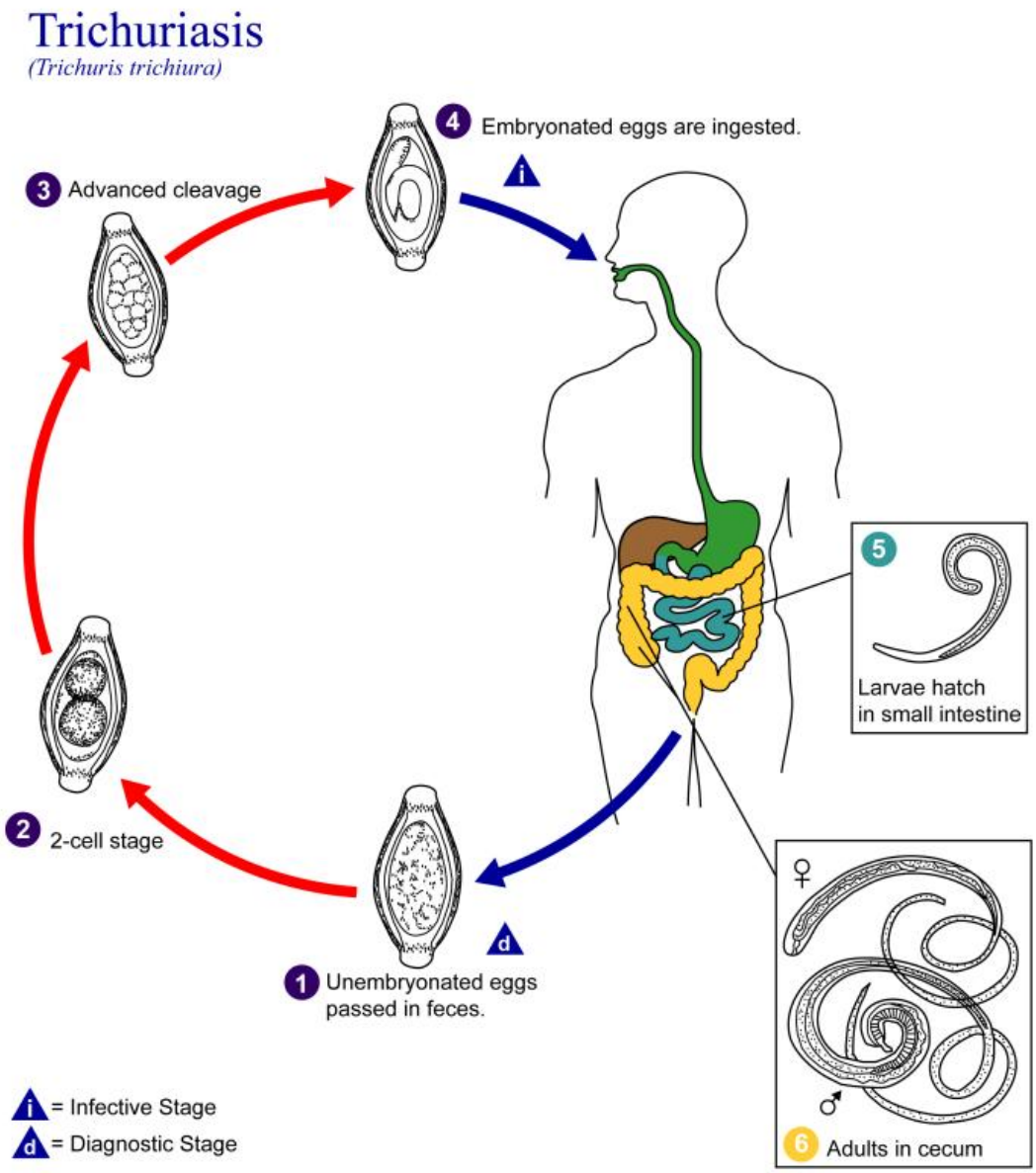


Figure 1-7: Life cycle of *Trichuris trichura*

(https://www.cdc.gov/parasites/trichuris/biology.html)

Infection with hookworm occurs when Larvae (L3) stage of the worm burrow through the skin of people walking bare feet (WHO, 2012). There are two types of hookworm, *Necator americanus* and *Ancylostoma duodenale*. The eggs pass out with faeces to the environment. The hookworm larvae are active, they leave the faeces and burry themselves in moist damp soil. These larvae

stages are called *rhabditiform* and are not infective, as they have to change into the sheathed filariform stage which takes about 5 days. These filariform larvae usually attach themselves to grass or hide in the soil, and in the event that they have contact with a human foot, they attach themselves to it and penetrate vigorously through the skin, and get to the lungs through the venous system and the right side of the heart. Once inside the lungs, they are carried up passively trough bronchiole, bronchi and trachea to the laryngiopharynx, where they are swallowed and reach the duodenum in 3-5 days after penetrating the skin. It takes about 40 days for the worms to attain adulthood and later attach to the intestinal mucosa with the teeth in their buccal cavity (Nordberg, 1999). The cycle is illustrated in Figure 1-8 below.

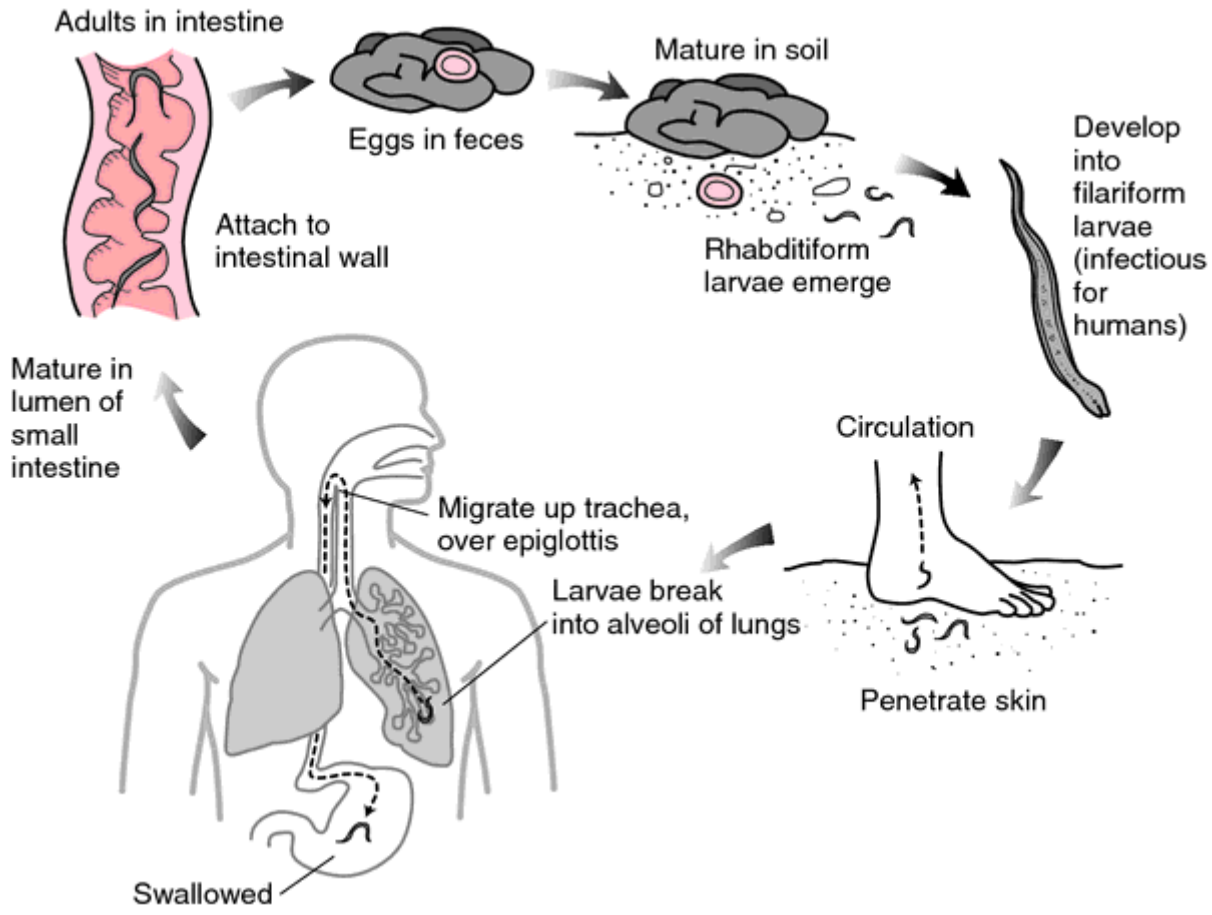


Figure 1-8: Life Cycle of Hookworm

(https://medical-dictionary.thefreedictionary.com/hookworms)

1.1.4 Pathological manifestations of STH

Since infection occurs not only at one time but repeatedly, a great number of worms could be found in one individual. This will eventually lead to a chronic form of the disease and long lasting health problems if the situation is not rapidly addressed. STH are known to cause malnutrition and this could either be due to loss of appetite so the child eats little amount of food, or by malabsorption once the food has been eaten (WHO, 2014).

Children who suffer from chronic worm infections and large numbers of worms usually exhibit signs of being stunted and underweight. The common symptoms observed in children with one or more kind of worm may include: loss of appetite, bloated and painful abdomen, coughing, fever, vomiting, diarrhoea, and a general feeling of unwellness (WHO, 2014).

Intense infection with roundworm can lead to bowel obstruction. Helminthes in particular hookworm can also be responsible for anaemia. Heavy worm burdens will automatically lead to frequent illnesses in children resulting in school absenteeism and poor academic performance. It is worth noting that chronic infections may lead to long-term retardation of mental and physical development, and death in very severe infections (WHO, 2014).

1.1.5 Prevention and Control of STH

Prevention of STH is multifaceted and includes first and foremost education on these infections, provision of safe water supplies, amenities for safe faeces disposal, hand washing facilities and prevention of faecal contamination of food.

Prevention and control should focus on;

- Availability and proper use of latrines.
- Provision of safe water and hand washing facilities after using the toilet and before handling food
- Careful washing fruits and vegetables with safe water before eating
- Training of children on the use of toilets and latrine
- Appropriate disposal of young children's faeces into latrines
- Wearing shoes and protective gear e.g. gloves when in contact with soil to prevent hookworm infection
- Cementing the floor of a latrine (Nordberg, 1999).

Treatment of STH

The World Health Organization (WHO) has recommended one of four antihelminthics namely; albendazole, mebendazole, levamisole or pyrantel for the control of STH infections.

In Kenya control of STH has been greatly enhanced by The National Deworming programme. The programme begun in 2012 and has substantially reduced STH infections, the overall prevalence of STH infections reduced to 16.4% from 32.3% within a period of three years (Okoyo *et al.,* 2016)

1.1.6 Life cycle of Schistosomiasis

Infection with schistosomiasis occurs when individuals come into contact with cercariae infested water. Water contact activities include children or adults wading, bathing, swimming or simply playing in ponds, rivers or lakes that have been contaminated with urine or faecal matter from an individual infected with schistosomiasis. Cercariae Infested water usually also contains fresh water snails that are intermediate hosts of the schistosome parasites (UNESCO, 2004). The life cycles of human urinary and intestinal schistosomes are very much alike, as illustrated in Figure 1-9. The adult schistosome worms live in blood vessels surrounding the bladder (urinary form) or intestine (intestinal form). The eggs of both *S. haematobium* and *S. mansoni* have spines on their wall; therefore some of the eggs break through and enter the walls of the intestine or bladder which leads to blood in the urine. The eggs are then passed out with the urine or faeces. Due to unsanitary practices by the infected individual, urine or faeces may end up in water where eggs are released. Under the right environmental conditions the eggs hatch into small active larvae called miracidia. The miracidia then infect specific fresh water snails of genus *Biomphalaria* for *S. mansoni* and snails of genus *Bulinus* for *S. haematobium* where they develop and multiply into successive generations of mother and daughter sporocyst. A subsequent type of larvae, called cercariae is then released from the infected snails. The cercariae can penetrate the skin of an individual who comes into contact with the cercariae infested water. They transform into schistosomular, then travel through the blood to the liver, where they undergo further growth and development (UNESCO, 2004). The male and female schistosomes pair up. *S. mansoni* paired adults migrate to the mesenteric venules of the bowel, laying eggs that are shed in stool while *S. haematobium* migrate to the venous plexus of bladder , laying eggs that are later excreted in urine (CDC, 2012).

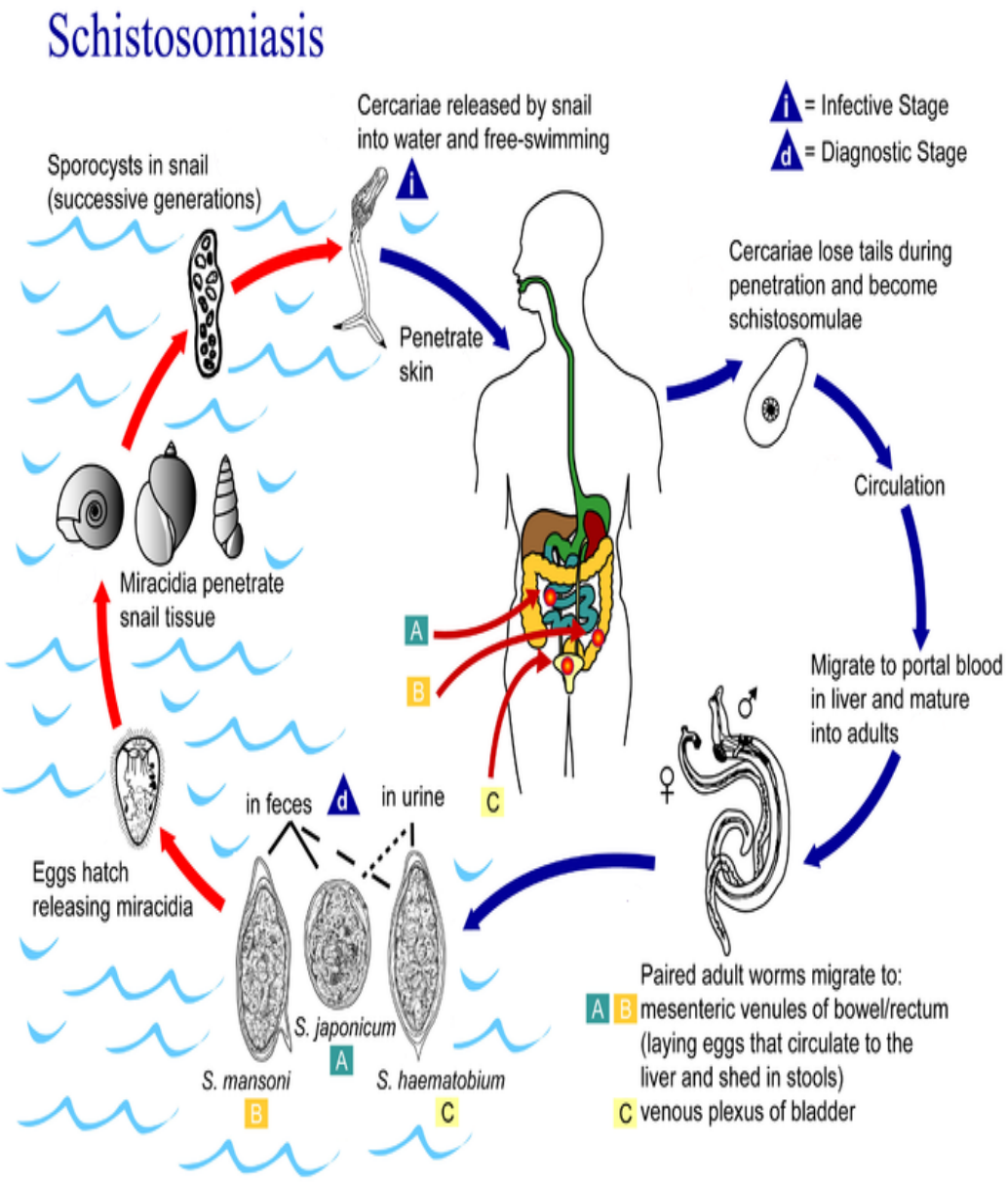


Figure 1-9: Life cycle of Schistosomiasis (CDC, 2012)

1.1.7 Pathological manifestations of schistosomiasis

Symptoms of disease associated with schistosomiasis are stage specific in relation to infection. In individuals who have had previous exposure, host response due to type of immunity and worm load, elicit different types of symptoms. Signs and symptoms of infection include dermatitis at the site of cercariae entrance into the body, an acute form of schistosomiasis also known as katayama fever and the chronic form of disease associated with tissue damage resulting from egg deposition. It has been observed that schistosomiasis has a negative influence on the nutritional reserves and development of humans from middle childhood through adolescence (Garcia, 2007).

In the invasion stage the cercariae penetrate the skin. This causes cercarial dermatitis with itching papules and local oedema. In many infections cercarial dermatitis goes unnoticed and is often not reported. The schistosomes mature in the liver. This stage of development is associated with fever, eosinophilia, abdominal pain and transient generalized urticaria. It is known as katayama syndrome (Nordberg, 1999).

Established infection is the stage at which eggs are produced by the adult worms. Pathology at this point is not due to the adult worms, but to the eggs that they produce. For both the urinary or intestinal forms of schistosomiasis only about half the eggs produced by the adult worms leave the body in the faecal matter or urine, as previously described in the life cycle (Nordberg, 1999). The other fraction of eggs moves further down the small veins of the bowel or bladder wall. Some eggs penetrate the tissues with the help of their spines while others are carried by the blood stream to the liver and lungs a fraction of the eggs fail to reach the lumen of the bowel or bladder. The eggs which do not reach the lumen provoke an inflammatory reaction and the formation of granulomas. It is this inflammatory reaction that is responsible for the early signs and symptoms of schistosomiasis; colitis with bloody diarrhea and abdominal pain in *S. mansoni* infection; haematuria and dysuria in *S. haematobium* infection (Nordberg, 1999).

Symptoms of the late stage of the disease include fibrosis and calcification which occur where many eggs are found in the tissues. If this occurs around the bladder it may result in: obstruction to and dilation of the ureters and kidney, with the probability of kidney failure; calcification of the bladder. In the liver, the fibrosis is periportal, resulting in portal hypertension. Portal hypertension leads to hyperplenism and anaemia, esophageal varices and often massive bleeding. In the lungs, the fibrosis results in pulmonary hypertension and in the heart the fibrosis leads to Congestive Heart Failure (CHF) (Nordberg, 1999). In school going children chronic cases can lead to retardation in growth, poor academic performance and school absenteeism (UNESCO, 2004).

1.1.8 Prevention and control of Schistosomiasis

The most efficient way to protect humans from schistosomiasis is health education. One important and fundamental way of controlling schistosomiasis is through proper fecal matter and urine disposal. The use of toilets and pit latrines will theoretically decrease the infection of snails. Nevertheless, only a small quantity of contamination of a water source, by an unsuspecting individual is needed to keep the vicious cycle of infection going. Therefore, it is mandatory to control snails as a major way of reducing transmission of schistosomiasis. The control of snails has proved to be a challenge in major schistosomiasis transmission zones in under developed and developing countries.

Schistosomiasis is increasing in endemic regions because infected water sources are the only available sources of water, therefore communities do not have alternative safe water for use. Schistosomiasis is also increasing due to agricultural practices like increase of land and communities under irrigation. Irrigation schemes form a perfect breeding site for snails and very often the introduction of irrigation practices is followed by an epidemic of schistosomiasis in that region (Nordberg, 1999).

The chemical agents that are effective in the control of snails are called molluscicides. But these agents are costly and need repeated application applied under close supervision in order to be effective in the control of snail vector populations. Molluscicides are disadvantageous, in that they are often toxic to humans and also kill fish. They ought to be applied during peak seasons of snail populations so as to ensure maximum kill. Recommended molluscicides should be effective and safe to handle; they should kill both snails and their eggs. The correct concentrations should be given, so that the chemical is not toxic to fish and plants. Niclosamide (Bayluscide) is equally safe to handle and use; it kills both snails and eggs. It is the cheapest chemical per volume of water but is likely to clog equipment (Nordberg, 1999).

Environmental hygiene is another control measure. Prevention of snail breeding may be used in combination to killing snails. This involves thorough alteration of snail habitats by draining or filling water bodies and clearing vegetation found in water bodies so as to deprive snails of food and their habitat. Ideally in irrigation schemes, intermittent irrigation results in sudden changes in water level and wave action. Flooding is detrimental for all snails; changing the speed of water flow in channels and rivers and leveling and deepening margins of water bodies are effective in clearance of snails. Ponds can be protected from snail intrusion. Sanitation engineers and public health specialists should be involved in the planning of irrigation schemes so as to control snail populations (Nordberg, 1999).

Treatment of Schistosomiasis

The antihelminthic praziquantel sold under the brand name biltricide is the drug of choice for treatment of infection with schistosomiasis. Praziquantel is also used to treat hydatid disease, tape worm infections, clonorchiasis and opithorchiasis. The drug is most effective against the adult worm therefore timing of treatment is very important (CDC, 2012).

The World Health Organization (WHO) focuses on target groups for treatment of schistosomiasis which are; children of school going age in endemic areas; adults living in endemic areas, and individuals whose occupations involve contact with contaminated water. The last category includes fishermen, farmers in contact with infested water, irrigation workers, and women whose household chores bring them in contact with cercariae infested water (WHO, 2015). The ideal strategy for schistosomiasis control focuses on disease reduction through regular treatment of targeted groups with praziquantel.

The regularity of treatment should be determined by the prevalence of infection in school-age children. In high endemic areas, treatment can be repeated yearly. Continuous monitoring of the infection status is important to evaluate the immediate and long term effect of treatment. However, the major impediment to schistosomiasis control has been the logistics involved in distribution of praziquantel; data reveals that in 2012 only 14.4% of people in need of treatment were reached. Praziquantel is effective and safe to administer (WHO, 2015). It is highly likely that re-infection will occur after treatment but with regular treatment the potential of developing severe illness is decreased and even reversed when treatment is started and repeated in childhood (WHO, 2015). Schistosomiasis has been successfully interrupted in Morocco. Countries like Egypt, Mauritius, Brazil, Saudi Arabia, China and Cambodia, have over the past 40 years successfully implemented schistosomiasis control (WHO, 2015).

1.1.9 Immunological aspects of schistosomiasis

During the process of infection with schistosomiasis in a human host, the immune system of the infected host has to tackle the life cycle stages of the parasites. These life cycle stages which include; the penetrating cercariae, migrating schistosomular, adult worms and the eggs produced by adult worm pairs, express hundreds of antigens (Lui *et al*., 2006,Verjovski *et al*., 2004 and Hokke *et al*., 2007). These antigens stimulate strong humoral and cellular immune responses. Different studies show that these responses continue to build up in the course of chronic infection, and others are strongly down-regulated (Leenstra *et al.*, 2006, Vereecken *et al.*, 2007 Naush *et al*., 2011 and Fitzsimmons *et al.*, 2012).

Schistosomes can live and mate in the human host without causing any harm and only eliciting immunological reactions when their eggs are trapped in the tissues of the liver or bladder. At this point, strong granulomatous T-cell mediated reactions lead to fibrosis in the liver and nodules and to a greater extent cancer of the bladder (Playfair, 1987). The adult worms evade immune attack by covering their surface with antigens derived from host cells, at the same time stimulating antibody which may destroy subsequent infections at an early stage. Schistosomes also secrete a variety of molecules, e.g. soluble lymphatic factors which interfere with and destroy host antibodies and inhibit macrophages making the destruction of the adult worm impossible. The combination of adult survival with killing of young forms is referred to as ‘concomitant immunity’ (Playfair, 1987).

Morbidity due to immunology

In human schistosomiasis morbidity is as a result of chronic immune stimulation by schistosome eggs that are trapped in tissue, resulting to granuloma formation and consequently fibrosis (Andrade *et al.*, 1971 and Kamel *et al*., 1978). The immense burden of disease due to *S. mansoni* and *S. haematobium* is attributed to chronic inflammation, resulting in morbidities such as anaemia, growth deficiencies, physical fatigue and diminished cognitive development (King *et al*., 2005, Leenstra *et al.*, 2006, Ellis *et al.*, 2008, Bustinder *et al*., 2011 and Butler *et al.*, 2012). The chronic inflammation is a type of innate immune response to the soluble egg antigens released from eggs trapped in tissue eggs (von Litchtenbeg *et al.*, 1994). In *S. haematobium* infections, anaemia due to chronic inflammation is aggravated by the blood loss seen as gross and micro-haematuria. In addition to direct morbidity, schistosome infections can have indirect consequences such as predisposition of the infected hosts to susceptibility to other pathogens. Studies have revealed that the sandy patches seen in female genital schistosomiasis caused by *S. haematobium* infections are associated with an increased risk of HIV acquisition (Kjetland *et al*., 2006 and Downs *et al*., 2011).

In the event that the immune process of granuloma formation if left unhampered, it would occupy enormous amounts of tissue space, eventually blocking the return of blood circulation back to the heart through the portal system resulting to portal and pulmonary hypertension and ultimately esophageal varices, consequentially leading to death. Before regular treatment with praziquantel of communities engaging in high-risk occupations, this morbidity and eventual mortality was observed in proportions of 2%-25% of those infected with either *S. mansoni* or *S. japonicum* (Ritcher *et al.*, 2003). This proportion can be attributed in part to immunomodulation of responses to SEA, as seen in reduced lymphocyte proliferation in patients that do not develop hepatosplenomegaly (Colley *et al.*, 1986). This occurrence has been observed in a number of

studies on human schistosomiasis, which all seem to conclude that constant continuous exposure to SEA results to the initiation of mechanism that down regulate granuloma formation, anti-IgE antibody production, and SEA-induced lymphocyte proliferation and cytokine production (Colley *et al* 1986, Grogan *et al*., 1998, Maizels *et al*., 2003, Malaquias *et al*., 1997 and Shen *et al.*, 2002). Studies of individuals in endemic areas have shown that down-regulation of SEA responses occur during chronic schistosomiasis and contribute to the establishment and ability of an infected individual to maintain chronic infections for years without developing hepatosplenomegaly (Colley *et al.,* 1998 and Richter *et al.,* 2003). In addition, immunogenetics can be attributed to the ability of individuals to regulate their immune responses to schistosome infections (Booth *et al* 2006 and Rodrigues *et al.,* 1996).

The idea that schistosomiasis infection during pregnancy might pass on an altered immune status on the offspring has been studied over time (Colley *et al.,* 1999, Lewert *et al.,* 1996 and Zhao *et al*., 2013). There is evidence that substantial passive immunity occurs in humans because newborns of mothers infected with schistosomiasis express IgM or and IgE antischistosome antibodies (Novato *et al*., 1992 and Seydel *et al.,* 2012). It can therefore be hypothesized that this expression of immunoglobulins may result in an early immunoregulation against SEA, allowing the majority of children in an endemic area to establish regulated, chronic infections (Colley *et al.,* 1999 and Djuardi *et al*., 2011).

Immunoglobulin E.

IgE has only been found in mammals. Like other immunoglobulin types, IgE is produced by B cells and plasma cells. In contrast to other immunoglobulin types, the concentration of IgE in the blood circulation is very low (Winter *et al.,* 2000). IgE in cord blood usually measures less than 1 U/mL (1 U 5 2.4 ng). Generally, adult IgE levels are achieved by 5 to 7 years of age. Between the ages of 10 and 14 years, IgE levels may be higher than those in adults. After age 70 years, IgE

levels may decline slightly and be lower than the levels observed in adults younger than 40 years (Winter *et al.,* 2000). Circulating IgE concentrations are very low because mast cells have a very high affinity for IgE (1010 mol/L21) via their e-heavy-chain Fc receptors (FceR). The synthetic rate for IgE is also very low. Immunoglobulin E attaches to mast cells and to basophils and activated eosinophils (Winter *et al.*, 2000).

IgE is the major immunoglobulin involved in immunity to parasitic helminths (Erb Kj, 2007) like *Schistosoma, Trichinella spiralis,* and *Fasciola hepatica* (Pfister *et al.*, 1983; Watanabe *et al.,* 2005; Fitzsimmons *et al.*, 2006).

Role of IgE in Schistosome infection

IgE plays a vital role in host immune protection against parasites. The role of IgE was first found by studies carried out on the cell mediated killing of schistosomes, as well as by epidemiological surveys in areas with endemic schistosomiasis (Sutton and Gould 1993). Studies showed that after the first 4-5 weeks of exposure to cercariae; when host immune system is aimed at worm antigens, the immune response is primarily Th1 in nature. During normal infection after eggs of schistosomes are produced, the immune response becomes highly Th2-polarized and after this the development of Th2 response follows. At this stage, there are increases in both plasma IgE levels and the number of circulating eosinophils, which mirror the production of Interlukin 4 (IL-4) and Interlukin 5 (IL-5). These are the key cytokines of Th2 cells that assist in class switching of B cells to IgE isotype and play the role of growth and survival factor for eosinophils, respectively (Pearce *et al.,* 2004).

Past studies have shown that resistance to reinfection may be due to the protective effect of IgE against adult schistosome antigens (Butterworth, 1994). Th2 cells play a very important role in the

production of IL-4 and IL-5 that is responsible for the expansion of high level of anti-parasite IgE in patients with schistosomiasis infection (Dutra, 2002). Antibodies of IgE isotype play a major role in protection against schistosomiasis by macrophage mediated toxicity. As illustrated in Figure 1-10 below experiments have also shown that eosinophils are major effector cells that can destroy *S. mansoni* in the presence of specific IgE antibodies (Janeway *et al.*, 2001).

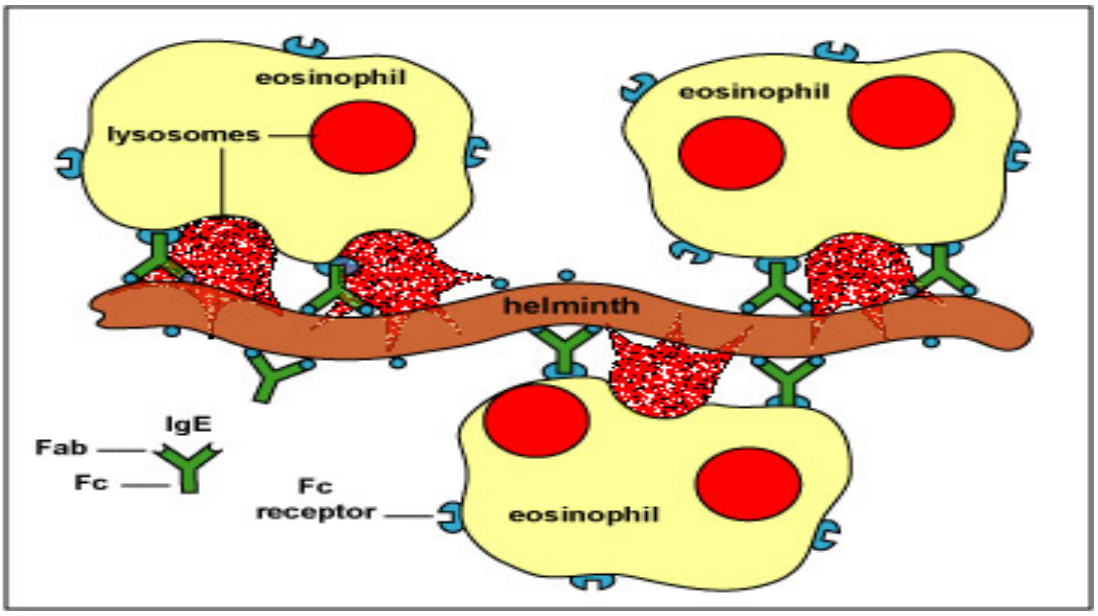


Figure 1-10: Opsonization of a helminth by IgE and Eosinophils.
(www.mdfaconline.org/bios/kaiserbio.html)

Th2 cells express Cytokines and CD4 ligands that stimulate B lymphocytes to express specific antibodies called IgE. IgE operates as an opsonizing antibody that attaches phagocytic eosinophils to helminthic worms and permit the release of major basic proteins. IgE also enables eosinophil cationic proteins to be focused on the targets for extracellular destruction of the helminthes. The Fab portion of IgE identifies epitopes on the helminth worm, whereas the Fc portion attaches to Fc receptors of activated eosinophils. The lysosomal proteases of eosinophils are able to tear down the tough integument of helminth worms. IgE also promotes inflammation to recruit phagocytic cells (Janeway *et al.*, 2001)

Resitance to Infection

The question of natural resistance to reinfection exists in certain individuals has long been discussed (Warren *et al* 1973), but a number of studies now signify that resistance to infection develops over a protracted period of time (Fitzsimmons *et al* 2012 and Mutapi *et al* 2013) . Some studies propose that worm death, either occurring naturally or after treatment, leads to the release of immunoglobulins that stimulate protective responses, which after a suitable number of occasions are in a position to effectively react with antigens expressed by susceptible incoming schistosomular (Fitzsimmons *et al* 2012, Walter *et al* 2006, Karanja *et al* 2002, Mwinzi *et al* 2009, Black *et al* 2010, Mutapi *et al* 1998, Mutapi *et al* 1999, Wilson *et al* 2013 and Pinnot *et al* 2013). Evaluating reinfection rates in people with different histories of exposure, contact with water bodies and differences in transmission intensities can be a major challenge.

In majority of endemic regions epidemiologic data of infected populations in general support age-associated decreases in infection as a consequence of development of antiparasite immunity (Mitchell *et al* 200). Recent studies indicate that certain *S. mansoni* adult worm-associated tegumental-allergen-like (TAL) proteins have been portrayed as important potential targets of protective IgE and reinfection-associated IgG4 (Walter *et al* 2006, Webster *et al* 1996 and Pinnot de Moira *et al* 2010). Studies have proved that cytokine responses to schistosome antigens are also enhanced by treatment. IL-4 and IL-5, cytokines associated with stimulation of IgE and eosinophil production, respectively, generally increased after praziquantel treatment (Roberts *et al* ,Scott *et al* 2000, Joseph *et al* 2004a,Joseph *et al* 2004b,Fitzsimmons *et al* 2004 and Grogan *et al* 1996). Other studies indicate that resistance to reinfection has been associated with these responses to the tegument antigen paramyosin in individuals infected with *S. japonicum*, and soluble adult worm antigen preparations in individuals infected with *S. haematobium* (Leenstra *et al* 2006 and Medhat *et al* 1998) The association between parasite-specific IgE, eosinophils and

resistance to reinfection has been observed across infective schistosome species in a variety of epidemiologic settings (Jiz *et al* 2009,Dunne *et al* 1992,Hagan *et al* 1991, Rihet *et al* 1991,Demeure et al 1993, Satti *et al* 1996 and Zhaosong *et al* 1997). Further research on the protective role of IgE have revealed that high and low affinity IgE receptors, on eosinophils and B cells (or in soluble form), respectively, are associated with protection against reinfection (Mwinzi *et al* 2009,Gounni *et al* 1994 and Ganley *et al* 2006).

1.2 Literature Review

1.2.1 The burden of disease and the effect of deworming

Approximately 240 million people worldwide suffer from schistosomiasis and more than 700 million people live in schistosomiasis endemic areas (WHO, 2014). In terms of mortality it is estimated that more than 200,000 deaths per year occur in Sub-Saharan Africa due to schistosomiasis (WHO, 2014). Morbidity due to helminthes is gradually being recognized as a major public health problem, particularly in developing countries where prevalence of infection is considerably high. Schistosomiasis and soil transmitted helminthes tend to be more prevalent in the less advantaged communities where poverty, malnutrition, lack of sanitation, unsafe drinking water and lack of health care is evident. Schistosomiasis and STH can infect and affect all individuals in a community but the most vulnerable group and the ones with the highest rate of prevalence are often children between the ages of 5 - 15 years. In children schistosomiasis has been known to cause anaemia, organ damage, stunted growth, impaired cognitive function and reduced academic performance (WHO, 2015).

Soil-transmitted helminth infections do not only infect African communities but are also cosmopolitan. According to CDC a great part of the world's population is infected with one or more of soil-transmitted helminths in which approximately 807-1,121 million people have Ascaris, 604-795 million have whipworm, and 576-740 million have hookworm (CDC, 2014).

A study conducted among school children in Abobo area, Gambella, in Ethiopia revealed an overall prevalence of urinary schistosomiasis among school children at 35.9% (Galeta *et al.,* 2014). In a prevalence study of 210 school children aged 7 to 15 years conducted in Senegal, 121 children (57.6%) were found to be infected with a mean geometric count of 185 eggs per 10 ml of urine. The prevalence of disease ranged from 14.3% to 92.8% in all the surveyed villages (Senghor *et al.,* 2014).

Double infection with *S. mansoni* and *S. haematobium* has been observed in some endemic areas. A study conducted in Yemen showed an overall prevalence of schistosomiasis infection of 24.8%. Out of the 614 school children enrolled in the study 183 (31%), were found to be positive with *S. mansoni* infection whereas 114 (18.6%) were found to be positive for *S. haematobium* infection. Double infection with both species was found in 12 children (Abdulrab, 2013).

In Kenya, approximately six million people are infected with either urinary or intestinal schistosomiasis (Chitsulo, 2000). Schistosoma infection has been endemic in some regions of the country, especially in areas with water projects for irrigation, which provide a habitat for the snail intermediate host. In Mwea region of central Kenya schistosomiasis transmission was recorded shortly after the irrigation scheme was started in the 1950 (Mutahi and Thiongo 2005). A cross sectional study on a population of 310 children from eight primary schools in Mbita, Kenya revealed very high prevalence of *S. mansoni*. A total of 238 (76.8%) children were infected with *S. mansoni*, while seven (2.3%) had *S. haematobium*. All the children infected with *S. haematobium* had co-infection with *S. mansoni* (Nagi *et al.,* 2014). Similarly a study of children aged between one to fifteen years conducted in Usoma area in Kisumu County, revealed infection rates even in preschool children. Out of the 484 enrolled children, the overall prevalence *S. mansoni* for the study population was 39% (Verani *et al.,* 2011). A study conducted in three villages in the endemic region of Taveta 36 years ago, indicates that prevalence of schistosomiasis was high in Kenya's post-independence period (Katamine *et al.,* 1978); a total of 963 individuals examined for stool and urine showed a prevalence of 69.6%: 23.6% had *S. mansoni*, 28.6% *S. haematobium* while 14.7% had co-infection. The study also indicated that children display the highest rate of infection with schistosomiasis. The study further revealed that prevalences increase rapidly with age in children and reach a peak between the ages of 5 to14years then gradually decrease (Katamine *et al.,* 1978).

A recent survey conducted in Taveta among 470 primary school children revealed 44% infection rate by either *S. mansoni*, *S. haematobium* or co-infection with both species (Gouvras *et al.,* 2013).

A prevalence study conducted in Brazil revealed the advantage of conducting schistosomiasis prevalence survey using primary school age children (Pereira *et al.,* 2010). Children in the age group of 6-15 years, serve as a comparative analysis of prevalence in that infection prevalence in this age group demonstrated the highest positive correlation with overall population prevalence. This age group is useful both as a target group and a reference point as it is the age range established for formal schooling in Kenya and many developing countries where schistosomiasis is endemic. It is also worth noting that children in this age group were the main targets of World Health Assembly resolution WHA-54.19, whose member countries, including Kenya were committed to the minimum goal of providing diagnostic coverage and treatment for helminth infection to 75% of school-aged children in endemic areas by the year 2010 (WHO 2002). Incidence and prevalence of infection observed from children in this age group may be used to evaluate not only the health situation of schistosomiasis in the schoolchildren, but also the need for intervention in the community as a whole (Montresor *et al.,* 2002). It is also advantageous in that the school infrastructure reduces the operational costs for parasitological surveys and medication administration. This is because it concentrates activities in a specific physical space and, in addition, provides an excellent opportunity to reach non-enrolled children (Favre *et al.,* 2009). As noted critically in this study, targeting of this particular age group allows for the follow-up of the impact of treatment over the period of between one to three years before they leave primary school. Additionally, children who test positive serve as a good indicator that could lead to the identification of infected family members, including non-enrolled children (Massara *et al.,* 2006; Enk *et al.,* 2008). A study conducted in the endemic area of Minas Gerais, Brazil, validated the use of prevalence among individuals in the 7-14 year-old age group to predict *S. mansoni*

prevalence in the community, confirming that it can be used to guide treatment strategies in the endemic area (Rodrigues *et al.,* 2000).

Soil transmitted helminthes are endemic in many African communities, especially among children. A study conducted among 284 primary school children in a rural community in Imo State, Nigeria revealed the overall prevalence of STH infection was 30.3%. Hookworm had a prevalence of 94.2% and was found to be the most common STH (Odinaka *et al.,* 2015).

Lack of personal hygiene has played a major role in the infection status of STH in children. A recent study conducted in Bihar state India among 1279 school children aged four to seventeen showed that poor hygiene plays a key role in the infection of STH. Overall, 68% of the primary school children from class 1-8 were infected with one or more soil-transmitted helminth species. The prevalence of *Ascarias*, hookworm and *Trichuris* was 52%, 42% and 5% respectively. An alarming percentage of children 95% practiced open defecation and 61% of the children reported that after defecation, they most frequently use soil for cleaning their hands (Greenland *et al.,* 2015). A similar situation was observed in Ethiopia where prevalence of STH infection was compared among private primary school and Government school. The prevalence rate of STH infections in private and government schools was 20.9% and 53.5% respectively. Study findings showed that among the government schools 62.9% of the children practiced open defecation (Debalke *et al.,* 2013). In Kenya high STH infection has been recorded in the urban slum of Kibera among preschool and school age children (Davis *et al.,* 2014)

Co infections of STH and schistosomiasis are common in endemic areas. A study conducted in the Lake Victoria basin of Tanzania revealed that intestinal schistosomiasis, urogenital schistosomiasis, and STH infections are highly prevalent. The study revealed that out of a total of 5,952 school children from 36 schools whose stool and urine specimens were examined, 898 (15.1%) were positive for *S. mansoni*, 754 (12.6%) for hookworms, 188 (3.2%) for *Ascaris*

lumbricoides, and 5 (0.008%) for *Trichuris trichiura*. Out of 5,826 schoolchildren who provided urine samples, 519 (8.9%) were found positive for *S. haematobium* eggs (Siza *et al.,* 2015).

A recent study conducted among primary school children in the Tana Delta reveals heavy infection and co-infection of primary school children in this endemic area with *S. haematobium* and STH infections. These parasites were responsible for significant morbidity. The prevalences of *S. haematobium,* hookworm, *T. trichiura* and *A. lumbricoides* infection were 94%, 81%, 88% and 46 %, respectively (Njaanake *et al.,* 2015).

Regular treatment of children infected with schistosomiasis and or STH can lessen the disease burden and reduce the possibility of chronic disease and complications later in life. Regular antihelminthic treatment results to better health and nutrition for school age children and this in turn leads to more children enrolling in school, less absenteeism and increased primary school accomplishment (WHO, 2003).

A study carried out in Nigeria showed that the efficacy of praziquantel against *S. haematobium* infection was established. Out of 350 school children who took part in the study, 245 (70.0%) within the age group of 4 to 15 years tested positive for *S. haematobium*. All the infected children were treated with a single 40 mg/kg oral dose of praziquantel. The treatment was repeated after four weeks and a follow up at 12 weeks. Monitoring revealed that at week four, eight and twelve after treatment, the Egg Reduction Rates (ERR) were 57.1%, 77.6% and 100%, respectively. The ERR was notably higher among the children who displayed light infection compared to those who displayed heavy infection. The cure rate at weeks four, eight and twelve were 49.4%, 85.5% and 100%, respectively (Ojurongbe *et al.*, 2014). A similar study conducted in South Africa, revealed similar results. Treatment with praziquantel among infected children displayed a high efficacy at three weeks after treatment, the egg reduction rate was 95.3% and cure rate of heavy infections was 94.1%. At week 41 after treatment the overall cure rate was 80.7% (Saathoff *et al.,* 2004). In

terms of reduction in prevalence, a study conducted in central Sudan, proved that treatment with praziquantel is equally efficacious. A single dose of praziquantel significantly reduced the prevalence of *S. haematobium* infection by 83.3% (from 51.4% to 8.6%) one year after treatment (Ahmed *et al.*, 2012). In a meta-analysis of three small studies where 149 individuals were tested for STH infections prior to participation, it was observed that a single dose of deworming treatment caused a considerable increase in weight of approximately 0.6 kilograms. Deworming has been confirmed to considerably improve mid-upper arm circumference and skin fold thickness in positive cases following single dose treatment of infected individuals (Ahmed *et al.*, 2012). The results of deworming are amazing, as demonstrated by a large study conducted in India. Within a period of two years, six monthly deworming was able to prevent 82% of the stunting that occurs without intervention; the children who were dewormed also showed 35% greater weight gain (Awasthi *et al.*, 2000). A world economic situation report presented to the United States Congress in 2003 concluded that the treatment of primary school children in developing countries with deworming drugs can reduce absenteeism by 25%. These conclusions agree with data from United States school children, which revealed a 23% decrease in attendance in children infected with hookworm (Bleaky, 2003).

1.2.2 Humoral immune responses and the effects of treatment

IgE and age

In communities where schistosomiasis is endemic, it has been noted that infection intensities peak in early adolescence and decline afterwards, this observation is believed to be evidence that acquired immunity to infection can develop. Therefore studies have linked IgE antibody levels to worm antigens, which are responsible for resistance to reinfection (Caldas *et al* 2000, Dunne *et al* 1992a Dunne *et al* 1992b, Hagan *et al* 1991, Satti *et al* 1996, Li *et al* 2001). Further studies have

established that the IgE levels increase with age, while antibody levels to egg antigens generally decline or are unchanged (Webster *et al* 1997, Naus *et al* 2003)

A recent study in Kenya, conducted in a highly endemic area of the Lake Victoria region, Asembo bay, found that some children exhibited a phenotype indicative of resistance to *S. mansoni* reinfection by 8–10 years of age (Black *et al.,* 2010). It has been established that infections with schistosomiasis in the lakeside communities begin very early in life (Odogwu *et al.,* 2006). Some of the 8–10-year-old children in the lake Victoria-asembo study could have been infected as early as at age one by the time of their enrolment therefore allowing for an opportunity for them to have already experienced dying worms. The resistant phenotype was characterized by high schistosome-specific IgE levels and elevated levels of CD23+ B cells (Odogwu *et al.,* 2006).

IgE and gender

In addition, human studies have established that there are indeed gender-related differences in humoral immune responses. These findings have been reported for the three most common species of *Schistosoma* that infect man (Webster *et al* 1997, Remoure *et al* 2001)

IgE and treatment

Praziquantel is the most effective chemotherapeutic agent against schistosomiasis and has also been found to work in synergy with host immune response. Past studies have established that praziquantel can destroy adult worms' in tegument, stimulate flaccid paralysis of worms and expose internal antigens (Pax *et al.,* 1978). Human host humoral and cellular immune responses can be activated after exposure to these worm antigens. Studies have been conducted that establish the development of humoral response after treatment of schistosomiasis infection (Mutapi *et*

al.,1998 a). A study conducted among 57 children aged between 6-15 years old in eastern Zimbabwe, established that production of IgA and IgG2 was remarkably lower after treatment compared to before treatment (Mutapi *et al.,* 1998 a). This finding can be accredited to the fact that these antibodies are aimed at the glycanic antigens on the tegument of adult worms. It was noted that after treatment these antigens disappeared and the amount of IgA and IgG2 declined. On the other hand, the levels of IgE, IgG1 and IgG4 against SEA were significantly higher in post-treatment than the pre-treatment follow ups (Mutapi *et al.,* 1998 b). A study in Kenya on changes of human isotype responses to *S. mansoni* antigens following treatment indicated that no significant differences were observed between pre-treatment and post treatment isotype responses to egg antigens (Webster *et al.,* 1997). The study also showed that IgG subclass responses to adult worm antigens were considerably lower after treatment, while IgE levels against adult worm antigens were significantly higher after treatment than before treatment. Similar phenomena were observed in another study in which antischistosomular tegument IgG4 considerably decreased and anti- Schistosomular tegument (STEG) and anti-soluble worm antigen preparation (SWAP) IgE increased after treatment in a population that displayed resistance to reinfection. The resistant group was significantly older than the group susceptible to reinfection (Caldas *et al.,* 2000) indicating, immunity to reinfection with increasing age.

Repeated Praziquantel treatment of more predisposed children increases these immune responses toward protective levels (Black *et al.,* 2010). Research evidence proves that treatment of school children and adults with Praziquantel boosts immune responses associated with resistance to reinfection with schistosomes in endemic areas (Mutapi, 1998a, 2003).

More recent studies have shown that treatment with praziquantel has enhanced immune response quantitatively and qualitatively**.** A study conducted in an endemic area in Mashonaland East Province of Zimbabwe, showed that six weeks after treatment, all of the treated children were schistosome egg negative. It was further observed that adult worm and egg-specific IgE titers

increased significantly following treatment (Rujeni *et al.,* 2013). Other similar studies have showed that praziquantel treatment boosts the anti-worm IgE immune responses associated with protection in older individuals (Black *et al.,* 2010). This suggests that the 3-5 age groups may equally gain immunologically from praziquantel, which reduces reinfection in older children and adults by stimulating IgE responses (F Mutapi *et al.,* 2003; Black *et al.,* 2010).

Studies on reinfection after chemotherapeutic treatment of individuals infected with schistosomiasis have identified immune responses that play an important role in resistance to infection with schistosomiasis. High levels of IgE against adult worm antigens have been linked with resistance to reinfection (Dunne *et al* 1992, Hagan *et al* 1991, Satti *et al* 1996, Naus *et al* 1998, Grogan *et al* 1996).

Undoubtedly treatment of school age children and adults with, praziquantel has been shown to boost immune responses associated with resistance to reinfection with schistosomiasis in endemic areas (Mutapi *et al* 1998a, Mutapi *et al* 1998b)

IgE and Intensity of infection

Research studies conducted in schistosomiasis endemic areas have well demonstrated that the reactivity of anti-SWAP IgE increases with age (Naus *et al* 2003 and Webster *et al* 1997) on the contrary there have been no associations between IgE reactivity and the intensity of infection with *S. mansoni* (Webster *et al* 1997). Even though the relationship between schistosome-specific IgE and parasite burden has not been established in endemic areas, high levels of schistosome specific IgE have been often been associated with protection against re-infection (Hagan *et al* 1992 and Dunne *et al* 1992) (Rihet *et al* 1991,Dunne *et al* 1992,Caldas *et al* 2000 and Walter *et al* 2006). In highly endemic areas, the positive association of schistosome-specific IgE and $CD23^{+}$ B cells with resistance to *S. mansoni* has been observed even in children (Black *et al* 2010).

A recent study conducted in an *S. mansoni*-endemic area of Bahia, Brazil, also showed no significant difference in the levels of *Schistosoma*-specific IgE between individuals with different parasite burdens (Figueiredo *et al* 2012). Another study conducted in Zimbabwe, in an *S. haematobium* endemic area among children between the ages of 5-18 years found a significant negative association between the ratio of IgE/IgG4 and infection intensity (Mutapi *et al* 2011). These data also indicated that resistance against *Schistosoma* infection could be related to the IgE/IgG4 balance.

1.3 Problem Statement

Schistosomiasis and soil transmitted helminthes remain a public health challenge in developing countries even in the 21st century. The prevalence and immune responses before and after treatment of primary school children with single and dual infections (with both *Schistosoma mansoni and Schistosoma haematobium*) in hard-to-reach areas of endemic countries, have been less researched, reported and documented. Therefore the main aim of this study was to gather knowledge on the incidence, prevalence and intensity of single and dual schistosomiasis; and on soil transmitted helminth infections in Primary school children, in Taveta Sub-County. The study further assessed the impact of deworming in the short term period of eight weeks and in the longer period of one year after treatment. The study further delved into understanding the immune status of the children in terms of IgE levels before and in the period of eight weeks after treatment.

1.4 Hypothesis

1.4.1 Null hypothesis

There is no reinfection with schistosomiasis and STH, and there is no significant difference in the immune response of the school children before and after therapeutic intervention.

1.4.2 Alternative hypothesis

There is infection and reinfection of schistosomiasis and STH, and there is a significant difference in the immune response of the school children before and after therapeutic intervention

1.5 Research Questions

1. What is the infection status of schistosomiasis (*Schistosoma mansoni, Schistosoma haematobium*) and STH in the school going children in Taveta?
2. What is the difference between the infection and re-infection status of *Schistosoma mansoni, Schistosoma haematobium* and STH in school going children, within a period of eight weeks, and one year after treatment?
3. What levels of IgE profile will be elicited by the primary school children, who are positive for infection with single and dual schistosomiasis infection at baseline and eight weeks after treatment?

1.6 Research Objectives

The main objective of this study was:

To study the infection and reinfection status of mixed schistosomiasis infection and STH, and the IgE levels in school children before and after treatment.

The specific objectives of this study were:

1. To investigate the prevalence of schistosomiasis and soil transmitted helminthes in the school going children in Taveta.
2. To determine the efficacy of treatment of single and dual *Schistosoma mansoni, Schistosoma haematobium* and STH infection in school going children at eight weeks, and one year after treatment.
3. To study the IgE profile elicited in the primary school children, who are positive for single and dual schistosomiasis infection at baseline and eight weeks after treatment

1.7 Justification and Significance of the Study

It is evident that schistosomiasis and STH infections still remain an enormous public health problem in the 21st century. These infections are in the neglected group of diseases that among others play a major role in barring socio economic development in endemic countries. Intestinal parasite control programmes have been implemented in numerous areas within developing countries aimed at the control of morbidity and, in the long term at the reduction of transmission. Most of these programmes have operated through primary health care approach, with little attention being given to the outcome of treatment in relation to the prevalence, intensities and efficacy of treatment.

The Kenya National school deworming programme, is a programme investigating sixteen counties spread in four regions country wide, and provides an excellent opportunity to reach young children. The school deworming programme has been in operation for two years (2012-2014) before baseline data on the infection status of the school children was collected by this current study in Taveta. This study seeks to address the outcome of the school deworming programme in a three pronged approach:

Firstly this study endeavored to investigate the prevalence and intensities of Schistosomiasis and soil Transmitted Helminthes in the endemic area of Taveta.

Secondly this study aimed at understanding the effectiveness of treatment in the period of eight weeks and one year after treatment

Thirdly the study will gather knowledge on the effect of treatment on the IgE levels of the primary school children, including those with dual *Schistosoma mansoni* and *Schistosoma haematobium* infections.

CHAPTER 2

MATERIALS AND METHODS

2.1 Study Area

This study was conducted in Taveta Sub County. Taveta Sub County is located in Taita Taveta County in the coastal region of Kenya; it covers an area of 17,084.1 sq Km. The county experiences mean annual rainfall of 650mm per annum with temperatures averaging 23ºC. It has water resources such as Lake Chala, Lake Jipe and Mzima springs that supply the coastal region with water (www.maplandia.com). The site was selected because of the unique occurrence of mixed *Schistosoma mansoni* and *Schistosoma haematobium* infection, among the population especially in the primary school children.

The schools were located in different locations from Taveta town as follows; Kiwalwa is 6.5 Km South, Abori is 8.1 Km South, Eldoro is 11Km South and Lotima is 13Km South of Taveta town, at the Kenya –Tanzania boarder as shown in Figure 2-1. The study area is endowed with water sources, in Kiwalwa area there is a river Kiwalwa that boarders the school, the community around this area has constructed a canal that is right at the schools perimeter fence which is used for irrigation. Abori area in itself is a swamp, and the area experiences flooding during heavy rains. As one heads to Eldoro there is a river Abori. At the Kenya –Tanzania boarder there is a river as you head to Lotima called River Nyumba ya Mungu as shown in Figure 2-1. These water sources in particular Abori area, are used for farming, which include banana plantations and rice farming among other food crops.

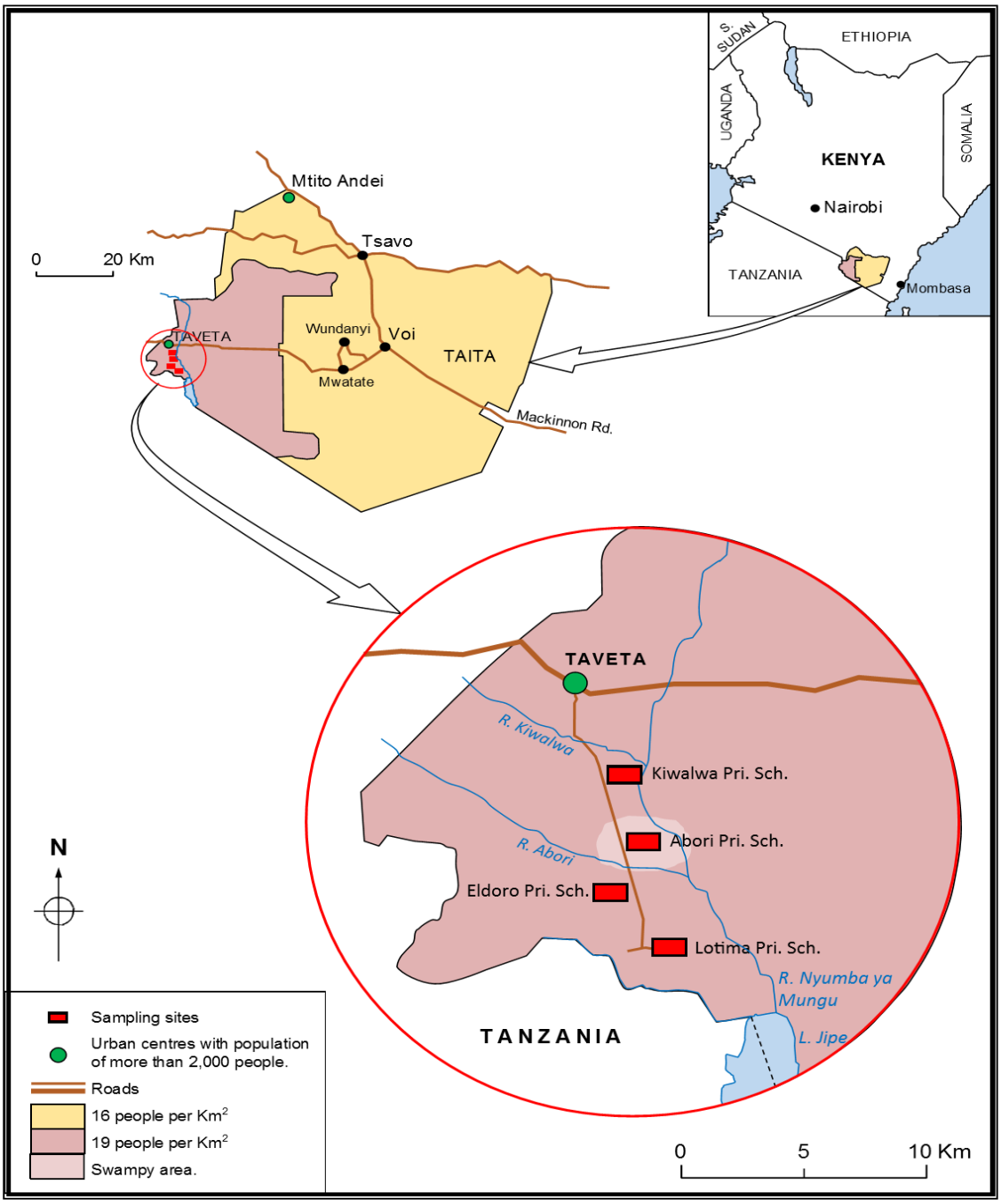


Figure 2-1: Map of the study area (Source: Google maps, Kenya 2017)

The map above indicates the sampling sites (schools) and adjacent water bodies.

2.2 Survey Investigations

Schools in communities adjacent to water bodies were preferred. The selected schools were visited 3 months prior to the survey date to have the purpose of the survey explained to the head teacher and class teachers concerned. An initial meeting was held with the County director for education and the primary school head teachers in order to solicit their cooperation and support.

2.2.1 Sample size

The formula by Fisher *et al.,* (1999) was applied to calculate the sample size:

Formula: $\mathbf{n} = \frac{Z^2 P Q (1 - P)}{d^2}$

When n= Minimum sample size required

Z = Confidence interval (1.96 the value corresponding to 95% confidence interval)

P = Estimated prevalence of *S. mansoni* among school going children (0.5) (Masaku et al 2015)

d^2= Absolute precision (Error margin)

Q = (1-P)

$n = \frac{1.96^2 x (0.5) (0.5)}{0.05x0.05}$

n=384

A minimum sample size of but not limited to 384 calculated from the Fisher formula was used for the study. The sample size was randomly selected from 4 primary schools in the study area. Pupils from class 1-5 were selected from both sexes using computer generated numbers. Stool urine and blood samples were collected from the selected pupils.

2.2.2 Collection, processing and examination of stool specimens

On the day of enrollment to the study, each selected pupil was given a container (poly pot) and instructed to place a portion of his or her own stool sample. The sample was then labeled with the child's identification number (ID) awaiting processing in the laboratory. Screening of infection for both soil transmitted helminthes and schistosomiasis was based on a double slide 47.1mg Kato-Katz smear (Peters *et al.,* 1980) prepared from fresh stool samples of each child, the equipment illustrated in Figure 2-2 below. The slides were left to clear for a minimum of 45min before microscopic examination, for the presence of ova. The slides were then systematically observed under a microscope for *Schistosoma mansoni, hookworm, Ascaris lumbricoides* and *Trichuris trichiura* eggs. The total numbers of eggs for each species were expressed as eggs/gm of feaces (epg). Quality control was performed by systematic random re-examination, by an experienced technician for 10% of the daily-examined Kato-Katz slides.

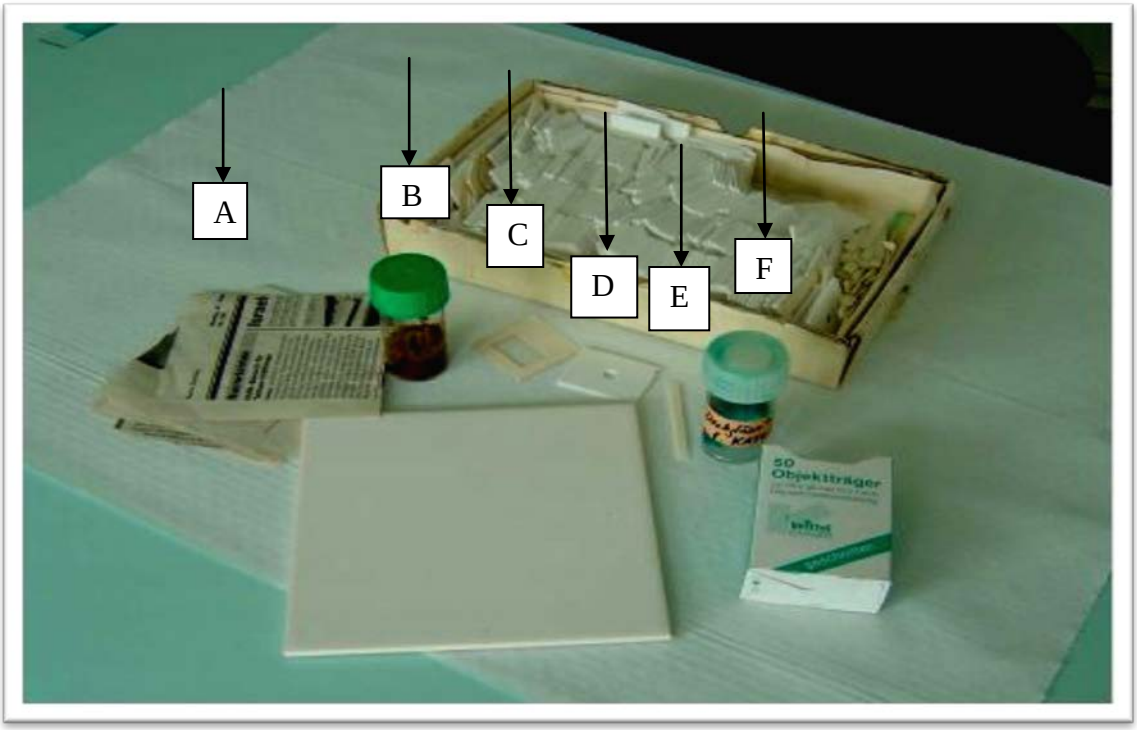


Figure 2-2: Kato katz Equipment:

The kit includes the following instruments used for processing stool; A. Newspaper, B. Stool, C. Sieve, D. Template, E. Applicator stick F. Cellophane

2.2.3 Collection, Processing and Examination of urine specimen.

Each selected pupil was also given another container to place a mid-morning urine sample in. The urine was then labeled using the child's ID. The urine sample was graded visually for presence of gross hematuria (visible blood in urine) on a scale of 1—6; 1 represented normal urine and 6 represented dark red blood in urine, with a grading of 4—6 indicating gross hematuria. Urine was then tested using the filtration method, whereby a 10ml disposable syringe without needle was used to draw urine from the urine container. The syringe was used to filter 10ml of urine through a 25mm filter with 20um pore (Nucleopore Corporation CA 94566) as indicated in Figure 2-3 below.

The filters were then observed using a microscope under x40 magnification for *S. haematobium* eggs. Prior to observation under a microscope, the filter was moisturized with a drop of normal saline to render the eggs visible.

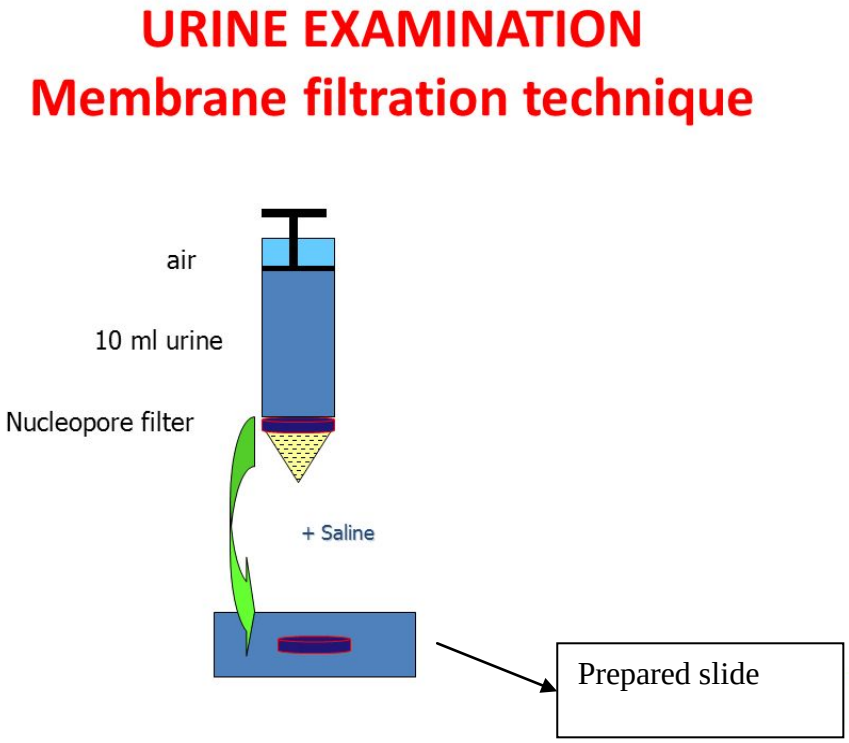


Figure 2-3: Membrane Filtration Technique

2.3 Assessment of drug Efficacy for mixed *S. mansoni* and *S. haematobium* Infections

After the first round of data collection was complete, all the children received treatment with a single dose of albendazole at 400mg for STH infection. The treatment was done in accordance to WHO recommendations. In schools where prevalence of either *S. mansoni* or *S. haematobium* exceeds 20%, all children (whether infected or not) should be treated with praziquantel at a dose of 40 mg/kg body weight.

Eight weeks after treatment of the school children and a year later, second and third round respectively of specimen collection and examination was conducted. The purpose of examination at eight weeks after treatment was to evaluate the efficacy of treatment, while at one year was to look at the re-infection levels at this particular time point. The efficacy of the treatment for each of the infections was evaluated based on the reduction in prevalence and intensity of infection. The Cure Rate, (CR) and the Egg Reduction Rate (ERR) were also calculated to measure efficacy of treatment according to the formula given in appendix 3. Intensity of infection, expressed as eggs per gram (epg) of feaces was classified according to the WHO recommended cut-off for low, moderate and high intensities of infection. For *A. lumbricoides* these were 1–4,999 epg, 5,000–49,999 epg and >49,999 epg for low, moderate and high intensities respectively. For *T. trichiura* the thresholds were 1–999 epg, 1000–9,999 epg and >9,999 epg for low, moderate and high intensities respectively, while for hookworms they were 1–1,999 epg, 2,000–3,999 epg and >3,999 epg for low, moderate and high intensities respectively.

2.4 Collection, processing and examination of blood specimen

Blood was collected at baseline to evaluate IgE levels before treatment and at eight weeks after treatment to evaluate the effect of treatment on IgE levels.

Children were asked to provide a finger-prick blood sample which was used to collect dry blood spot on Whatman filter paper. Commercially available Whatman filter paper no. 903 circular in shape having a diameter of 125 mm was used for blood sample collection (WHO Memorandum, 1974). Blood was collected as a spot on filter paper near its circumference by finger prick. After explaining the procedure to the school children and their parents and guardians, blood spots were taken from consenting pupils, as illustrated in Appendix 9. While taking aseptic precautions, blood was allowed to make a spot on filter paper by touching the filter paper at the site where prick was made as shown in Appendix 10. The filter paper was allowed to dry at room temperature for 45 min. After drying, each filter paper was kept in a zip lock paper bag containing desiccant and kept in a cooler box for transportation. In the laboratory the blood spots were stored in a freezer at -20°C awaiting the laboratory procedure.

2.4.1 Determination of antibody responses

The antibody detection and quantification was done using the Enzyme Linked Immunoabsorbent Assay (ELISA) technique (Rujeni *et al.,* 2013). Slight modifications were done after optimization and standardization. In this technique, antigens are loaded on a plate. An antibody conjugated to an enzyme is added. Binding of antibody and antigen is detected by adding a substrate whose break down products after enzymatic reactions give color. This color is detected by ELISA reader.

Before the ELISA procedure the blood spot was punched out with the help of 10 mm paper punch. The punched filter paper was placed in a test tube and eluted with 250µl of Phosphate Buffered

Saline with Tween 20 (PBST) at 4°C for 24 hours. After 24 hours the test tube was gently vortexed for proper mixing. The eluted sample was used for *Schistosoma* serology using ELISA.

2.4.2 Method for ELISA

Wells of microtiter plates (Nunc Thermoscientific) were coated with 50ul/well of Soluble Egg Antigen (SEA) at 10ug/ml and 50ul/well of Soluble Worm Antigen (SWAP) 10 ug/ml in Phosphate Buffered Saline (PBS) 1x and incubated overnight at 4^0C. The plates were washed the following day 3 times with PBST and banged on a paper towel. The plates were then blocked with 100 µl/well of 3% Phosphate Buffered Saline – Bovine Serum Albumin (PBS-BSA) then incubated at 37°C for 1 hour. The plates were then washed 6 times with PBST. Eluted samples were then loaded into the plates in duplicate at 50ul/well at 1ug/ml and incubated for 2 hours at 37 °C. After incubation the plates were then washed 6 times with Phosphate Buffered Saline Tween (PBST). 50ul/well of Goat antihuman IgE Horseradish Peroxidase (HRP) conjugated antibody was added and incubated for 1 hour at 37 °C. After incubation 150ul/well of 1 step 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) were added to the plate, covered with a foil an placed in the dark for color change to develop.

All samples were assayed in duplicate; sera from positive children with schistosome infection were used as positive control while negative sera from volunteers in a non-endemic area were used as negative control. Ige Levels were expressed as optical densities. Optical densities greater than 0.01 were considered as positive IgE levels. The color was allowed to develop in the dark for 30 minutes as seen in Figure 2-4 below. Absorbance was then read using an ELISA reader (Biotek) at 630nm.

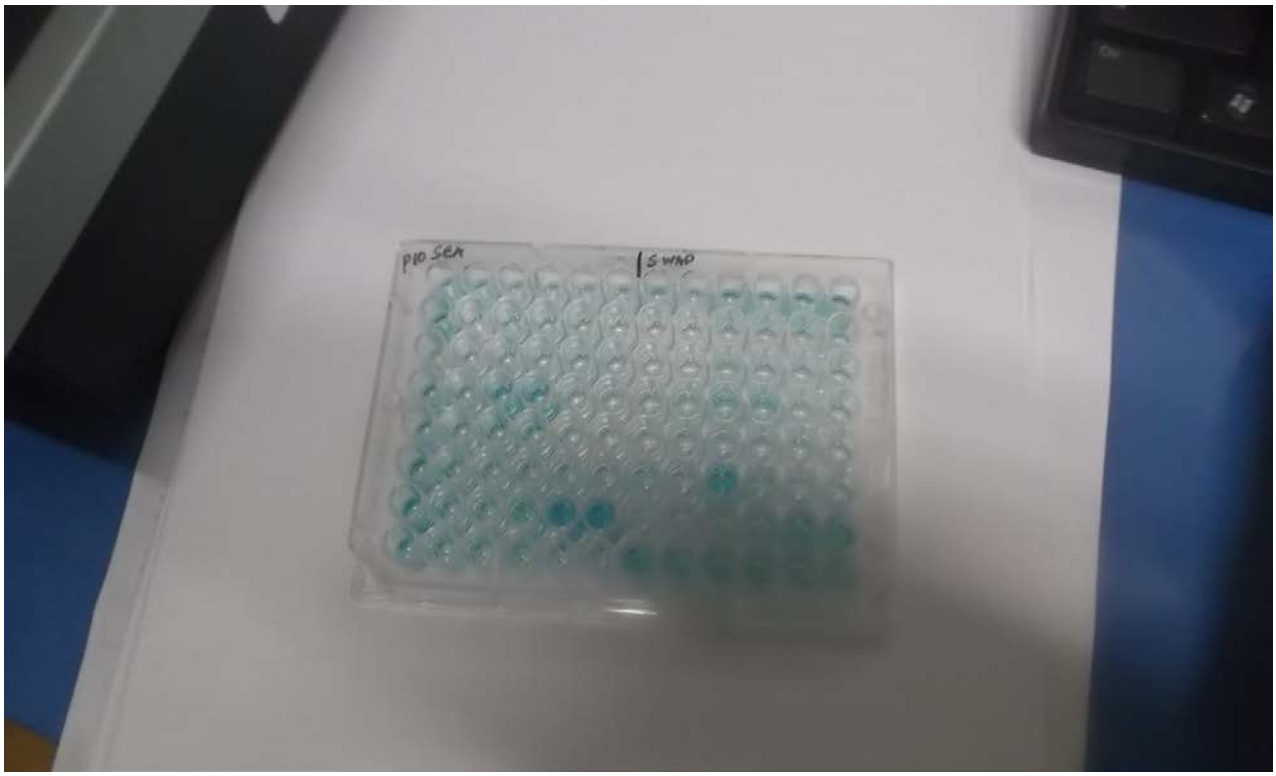


Figure 2-4: Microtiter plate

The pockets of developed color are am indication of antigen antibody reaction

2.5 Data Management

2.5.1 Data collection

Baseline data was collected from 442 primary school children in 4 primary schools in Taveta Sub County. This was done before the yearly Kenya National Governments' primary school deworming programme. During deworming, all the primary school children in Taveta Sub County are treated with a single dose of 40 mg/kg of praziquantel for schistosomiasis and another single dose of albendazole at 400mg/kg for soil transmitted helminth infections. After treatment data was collected from the same children eight weeks later in order to test for drug efficacy. One year after treatment, data within a period of one year after treatment to test for reinfection.

2.5.2 Data entry and storage

Data was collected on paper form, counter-checked for accuracy, and verified before double entry into a computer Excel 2007 spreadsheet. All statistical analysis was survey set and carried out using STATA version 12.0. All data does not contain recognizable names for confidentiality.

2.5.3 Data analysis

The observed overall prevalence of both *S. mansion* and *S. haematobium* were calculated by gender and age groups. Confidence intervals of 95% (95% CI) were calculated by binomial logistic regression. Differences in prevalence between the two species were calculated by the Wald test. The intensity of infection was calculated in the form of geometric mean eggs per gram of feaces. Comparison of prevalence by gender and age groups were tested on significance using the Fisher's exact test. The age's of the children were categorized in different age groups during analysis these were: 5-7, 8-10, 11-13 and >13 years old. The significance of the factors associated with infection of *S. mansoni* and *S. haematobium* in the school children was determined using the

multivariable logistic regression model reporting the odds ratio at 5% significance level and 95% confidence intervals. The choice of the model was based on the log likelihood function. Factors for the infection were selected using forward step-wise variable selection method. Differences in proportions by age, sex and school were assessed by logistic regression and differences in means using a chi-square test, relationships were tested by the correlation co-efficient. Risk ratio was used to calculate the risk of infection in the primary school children. This is the ratio of the cumulative incidence in the exposed and unexposed groups.

The Non Parametric Wilcoxon sum rank tests (Mann-Whitney U tests) for the independent samples were performed to compare before and after treatment of antibody- antigen reaction Optical Densities (OD). A quartile regression was performed to check the relationship of the optical densities and age. The test was conducted for two antigens namely SEA and SWAP

2.6 Ethical considerations

Ethical clearance for this study was sought from KEMRI's Scientific Steering Committee (SSC) and Ethical Review Committee (ERC) prior to commencement of activities. (Clearance letter provided at the end of the thesis)

2.6.1 The Recruitment strategy.

From the four schools in Taveta, children were enrolled by purely random sampling.

Computer generated numbers were used to select the children at random, and each child stood a chance of being selected. The selection exercise took place on the day of sample collection in the morning while the children were in the school assembly.

The children that were selected were put in a separate class rooms as the rest of the pupils were asked to go to their respective classes and continue with their normal class schedule and lessons. The children who were randomly selected and declined to take part in the study were automatically replaced. Before the random selection the students were informed that they had the right to accept or decline in participation and there would be no discrimination after that.

Specimens were collected in the school toilet facilities; the girls collected their specimen separately from the boys, i.e. each in their respective toilets.

2.6.2 Community consultation and informed Consent

The Kenya national deworming programme is an ongoing yearly activity that has been taking place for two years. Before the programme begun, the parents, teachers, school administration from county governments in endemic areas were informed of the programme.

Before every exercise in this study, meetings were held with the county government of Taveta, Department of Education, the teachers and the local district hospital, to inform them about the exercise.

Parents and guardians had the chance to ask questions and were informed that participation of their children in the study was completely voluntary and that they had the right to withdraw from the study at any time.

2.6.3 Biosafety consideration and risks

The stool was collected into stool sample containers using wooden tongue depressors while the urine was collected into urine containers. After collection, the specimen was put into cooler boxes and transported to the district laboratory for processing. The already processed stool was disposed

immediately into Biosafety plastic bags, together with the used poly pots. In the Laboratory human samples were handled with all due Biosafety precautionary measures.

Stool sample collection may be embarrassing for the children, but this discomfort was minimized by guaranteeing children's privacy during stool collection. During blood sample collection, a small prick was made through the finger of the child, this may have caused a small injury and pain onto the study subjects but this pain disappeared in a few minutes.

2.6.4 Confidentiality

All records were kept as confidential as possible. Participants were identified primarily by their study numbers and names were not entered into the computerized database. No individual identities were used in any reports or publications resulting from the study.

The data was accessible only to the principal investigator and the supervisors. Since the data is stored in computers, it is password protected

2.6.5 Benefits

The most immediate benefit of the study was free medical treatment for helminth infections. Mass treatment for STH infection with albendazole (400mg) was implemented by the Kenya government in all schools in endemic region. In schools where prevalence of *S. haematobium* exceeds 20%, all children (whether infected or not) were treated with Praziquantel [40 mg/kg].

CHAPTER 3

RESULTS

3.1 Introduction

This section comprises of statistical results based on the three specific objectives of this study. The first result is based on the infection status of schistosomiasis in the school going children, these includes prevalence and intensities of infection, and the relationship of the same with age and gender. This section also includes the prevalence of dual (*S. mansoni* and *S. haematobium*) infections. The second set of result focus on the efficacy of treatment of single and dual *S. mansoni* and *S. haematobium* in the school going children after eight weeks of treatment and one year of treatment respectively. Thirdly the analysis center on the IgE profile elicited in the primary school children, at baseline (before treatment) and 8 weeks after treatment. Further the analysis investigates the relationship between IgE antibody levels with age and intensities for single and dual infections. Finally this section presents the prevalence of infections with STH, which were minor in terms of prevalence and too low for adequate statistical analysis, but have been reported in Table 3-29.

3.1.2 Demographic characteristics of the study sample

Baseline data was collected from 442 children in the study area. The children were represented in both genders with the majority 227 (51.35%) being female and the male being 215(48.65%). Most 219 (49.15%) of the children surveyed were in age group of 8-10 years with the mean age of 9 years (SD ±0.09 yrs) and ranging from 5-16 years. There was an increase of 5 children at 8 weeks after treatment and a decrease of 45 children at 1 year after treatment, these differences were mainly insignificant

3.2 The infection status of schistosomiasis in the school going children

3.2.1 Prevalence

The overall prevalence of *S. mansoni* was 11.7% (95%CI 8.7%-14.6%), while that of *S. haematobium* was 24.4 % (95%CI 20.4%- 28.4%), respectively. The difference in prevalence between the two species was highly significant (Wald test) (P <0.001). The prevalence of *S. haematobium* was significantly higher in the male children as compared to the female children (28.8% vs. 20.3%, P-0.03). On the other hand, there was no significant difference in prevalence of *S. mansoni* between sexes, as seen in Table 3-1 below. The prevalence of *S. haematobium* was highest among the age groups 11-13 years at 26.8%, followed by the 8-10 years at 26.5 %. The prevalence of *S. mansoni* was highest among children older than 13 years at 20% and high among the age group of 11-13 years at 13.4%, followed by the 5-7 years at 13.2% (Table 3-1).

Table 3-1: The Prevalence of *S. haematobium* and *S. mansoni* by gender, age group and school in the study sample

	S. haematobium		***S. mansoni***	
Category	Prevalence (%)	95%CI	Prevalence (%)	95%CI
Overall (442)	24.4%	20.4-28.4	11.7%	8.7-14.8
Prevalence by gender				
Male (215)	28.8%	22.7-34.9	12.1%	7.7-16.5
Female (227)	20.3%	15.0-25.5	11.5%	7.3-15.5
Prevalence by age groups				
5-7(106)	17.9%	10.6-25.2	13.2%	6.7-19.6
8-10 (219)	26.5%	20.6-32.3	10.0%	6.1-14.0
11-13 (112)	26.8%	18.6-34.9	13.4%	7.1-19.7
>13 (5)	20.0%	0.0-55.1	20.0%	0.0-55.1
Prevalence by school				
Kiwalwa (139)	24.5%	17.3-31.6	5.8%	1.8-9.6
Abori (105)	25.7%	17.3-34.1	14.3%	7.5-21.0
Lotima (98)	21.4%	13.3-29.5	15.3%	8.2-22.4
Eldoro (100)	26.0%	17.4-34.6	14.0%	7.2-20.8

3.2.1.1 Prevalence among the schools

The prevalence of *S. haematobium* among the schools was highest in Eldoro primary school at 26.0% (95%CI 17.4%-34.6%) followed closely by Abori primary school at 25.7% (95%CI 17.3%-34.1%). It is notable that the prevalence of *S. haematobium* was over 20% in all the four primary schools. On the other hand, the prevalence of *S. mansoni* was highest in Lotima primary school at 15.3% (95%CI 8.2%-22.4%) and lowest in Kiwalwa with 5.8% (95%CI 1.8%-9.6%).

In an attempt to determine the association of *S. haematobium* and *S. mansoni* infections with gender and schools forward variable method was performed based on the multivariable logistic regression model.

It was observed that the female children were significantly less likely to be infected with *S. haematobium* compared to males (OR -0.4896, p-value 0.031). In terms of schools, the children in Abori, Lotima and Eldoro primary schools are significantly more likely to be infected with *S. mansoni* compared to children in Kiwalwa primary school (OR 1.03, 1.11 and 1.02, respectively $P < 0.05$).

3.2.2 Intensity of infections

The intensity of infection was estimated by the geometric means. For *S. mansoni* infection, this was expressed as eggs per gram of feaces (epg), and as eggs/10ml of urine for *S.haematobium*. The mean intensity for *S. mansoni* was 0.65 eggs per gram while for *S.haematobium* this was 1.16 eggs per 10ml of urine as shown in Table 3-2. The mean intensity among gender and different age groups are shown in Table 3-2.

Table 3-2: The geometric mean intensity of infection of *S. haematobium* and *S. mansoni* in the study sample

Infection	Mean intensity (Geometric)	95%CI	Standard deviation	Range
S. mansoni	0.65	0.45-0.88	±0.18	0-529
Gender				
Female	0.66	0.38-1.01	±0.18	1-337
Male	0.64	0.36-0.97	±0.17	1-529
Age group				
5-7 yrs	0.77	0.33-1.37	±0.30	1-217
8-10 yrs	0.53	0.29-0.83	±0.15	1-241
11-13 yrs	0.76	0.33-1.33	±0.29	1-529
>13 yrs	1.17	0.25-17.90	±0.97	1-49
S. haematobium	1.16	0.86-1.50	±0.17	0-1001
Gender				
Female	0.85	0.54-1.22	±0.18	1-1001
Male	1.54	1.00-2.22	±0.34	1-1001
Age group				
5-7yrs	0.82	0.35-1.43	±0.31	1-1001
8-10yrs	1.31	0.86-1.88	±0.29	1-1001
11-13yrs	1.27	0.67-2.06	±0.40	1-961
>13 yrs	0.24	0.00-1.29	±0.53	1-3

Further the intensity threshold for *S. haematobium* and *S. mansoni* was categorisized into heavy, moderate and light infections. This classification was based on the WHO criteria (WHO 2002) as shown in appendix 1a and 1b. The intensity of infection at the school community level was calculated. It was observed that for *S. mansoni* 0.22% had heavy intensity, 3.39% had moderate and 8.14% light of infection. For *S. haematobium* 7.23% had heavy intensity while 17.19% had light intensity of infection as seen in Table 3-3 below.Therefore this indicated that a large number of the pupils who tested positive for *S. mansoni* and *S. haematobium* had light intensity thresholds

Table 3-3: The intensity threshold of *S. mansoni* and *S. haematobium* among the study sample

	S. mansoni (n=442)		***S. haematobium(n=442)***	
	Prevalence	95% CI	Prevalence	95% CI
Heavy	0.22%	0.03%-1.28%	7.23%	5.67%-9.23%
Moderate	3.39%	1.54%-7.45%		
Light	8.14%	5.4%-12.2%	17.19%	14.52%-20.88%

3.2.3 Dual infections

Further analysis revealed that out of the 442 primary school children 24 (5.3%) had dual infection (both *S. mansoni* and *S. haematobium).* Among the children with dual infections; both sexes had almost similar prevalence. For the boys it was 5.11% while for the girls this was 5.72% as seen in Table 3-4 below. Although the dual infections did not differ significantly among the age groups, the 8-7 year's age group had the highest prevalence of dual infections followed by the 8-10 years age group. Children in the age group of 13 years and above did not have any case of dual infections.

Table 3-4: Prevalence of dual infection in relation to gender and age in the study sample

Category(n)	Prevalence	95% CI
Overall	5.43%	3.67%-8.01%
Prevalence by Gender		
Female	5.71%	3.37%-9.1%
Male	5.11%	2.87%-9.09%
Age category		
5-7 yrs	6.60%	3.95%-16.4%
8-10 yrs	5.93%	4.67%-13.3%
11-13 yrs	3.57%	1.36%-9.34%
>13 yrs	0.00%	

Further a multivariate logistic regression was done to check how age and gender factors had an influence the dual infection. None of these factors was found to significantly influence the infection of both *S. mansoni* and *S. haematobium.*

3.3 Efficacy of treatment of single and dual *S. mansoni* and *S. haematobium* infection in the school going children at eight weeks, and 1 year after treatment.

3.3.1 Prevalence of infection at eight weeks after treatment

Eight weeks after treatment the overall prevalence of *S. mansoni* was 1.13% (SD=0.5%, 95% CI 0.15%-2.12%), while that for *S. haematobium* was 5.58 %(SD=1.5%, 95% CI 2.63%-8.53%) respectively. Just like the baseline results these two infections differ significantly (exact test) with *S. haematobium* infection being significantly higher (P-value=0.001). The prevalence of *S. haematobium* did not differ significantly between boys (6.83%) and girls (4.31%). The prevalence of *S. haematobium* was highest among the age group of 8-10 yrs (8.0% 95% CI 2.33-13.76%). It is notable that *S. haematobium* infection was not prevalent among the 5-7yrs age group as seen in Table 3-5 below. During this survey there was no dual infection among the pupils.

Table 3-5: Infection status of *S. haematobium* and *S. mansoni* at eight weeks after treatment with Praziquantel.

	S. haematobium		***S. mansoni***	
Category	Prevalence %	95%CI	Prevalence (%)	95%CI
Overall	5.58%	2.63-8.53	1.13%	0-2.28
Prevalence by gender				
Male	6.83%	2.26-11.41	1.39%	0-2.84
Female	4.31%	0.61-8.00	0.90%	0-2.13
Prevalence by age groups				
5-7	0.00%		1.12%	0-3.31
8-10	8.00%	2.33-13.76	1.65%	0-3.59
11-13	5.68%	0.84-10.52	0.65%	0-0.91
>13	7.69%	0.0-22.18	0.00%	0.00

3.3.2 Intensity of infections

The mean intensity for *S. mansoni* was 0.05 epg while for *S. haematobium* was 0.15 eggs/10ml as seen in Table 3-6 below. The mean intensity among gender and different age groups are shown in Table 3-6.

Table 3-6: The geometric mean intensity of infection of *S. haematobium* and *S. mansoni* at eight weeks after treatment in the study sample.

Infection	Mean intensity (Geometric)±SD	95% CI	Range
S. mansoni	0.05 ± 0.025	0.00-0.10	0-265
Gender			
Female	0.04 ±0.061	0.00-0.10	1-265
Male	0.06 ±0.040	0.00-0.14	1-265
Age groups			
5-7 yrs	0.03 ±0.040	0.00-0.11	1-25
8-10 yrs	0.08 ±0.051	0.00-0.18	1-265
11-13 yrs	0.03 ±0.040	0.00-0.11	1-265
>13 yrs	0 ±0	0.00-0.00	1-1
S. haematobium	0.15±0.56	0.05-0.26	0-532
Gender			
Female	0.14±0.81	0.00-0.30	1-532
Male	0.16±0.76	0.40-0.31	1-64
Age groups			
5-7 yrs	0±0	0.00-0.00	1-1
8-10 yrs	0.26±0.14	0.03-0.54	1-532
11-13 yrs	0.11±0.06	0.01-0.23	1-14
>13 yrs	0.27±0.46	0.00-1.17	1-24

Intensity threshold

As can be seen in Table 3-7 below none of the infected children had heavy intensity for *S. mansoni*, in the period after treatment, while for moderate and heavy it was below 1%. It is

worth noting that 0.08% had heavy intensity for *S. haematobium* while 4.78% had light intensities.

Table 3-7: The intensity threshold of *S. mansoni* and *S. haematobium* at eight weeks after treatment among the study sample

	S. mansoni		***S. haematobium***	
	Prevalence	95% CI	Prevalence	95% CI
Heavy	0.00%		0.80%	0.70%-0.92%
Moderate	0.67%	0.17%-2.50%		
Light	0.44%	0.06%-3.17%	4.78%	1.99%-7.44%

3.3.3 Comparison of prevalence's at baseline and after treatment.

Overall relative comparison of prevalence between the baseline and eight weeks after the treatment is illustrated in Table 3-8 below. The prevalence of *S. mansoni* reduced from 11.76% to 1.12% and of *S. haematobium* reduced from 24.43% to 5.58% after treatment in duration of eight weeks. In both infections the reduction in prevalence was highly significant. In this study Cure Rate is defined as the proportion of children found positive with schistosome infection that turned negative after treatment with praziquantel. Cure rate for *S. mansoni* was 90.38% while the egg reduction rate was 92.31%. The Cure rate for *S. haematobium* was 87.9% while the egg reduction rate was 87.06% as seen in Table 3-8 below. As seen in Table 3-8 below, treatment reduced the risk of infection of *S. mansoni* by 9.5% while the risk of infection by *S. haematobium* is reduced by 22.83%.

Table 3-8: Prevalence, Cure rate (CR), Egg Reduction rate (ERR) and Risk Ratio (RR) of *S. mansoni* and *S. haematobium* at baseline and eight weeks after treatment

	Baseline	Eight weeks	(CR)	(ERR)	Risk Ratio	p-value	95% C.I of RR
S. mansoni	11.76%	1.12%	90.38%	92.31%	9.5%	<0.001	3.8%-23.5%
S.haematobium	24.43%	5.58%	87.96%	87.06%	22.83%	<0.001	13.1%-39.7%

3.3.3.1 Relative comparison of prevalence by gender

There was a significant reduction in prevalence of *S. mansoni* infection for both genders. Prevalence for the female pupils, reduced from 11.45% to 0.8%, while for the male pupils, the prevalence reduced from 12.09% to 1.13% as seen in Table 3-9 below. There was 92.30% cure rate and 88.46% cure rate of the female and male students respectively in the period eight weeks after treatment. There was 93.93% egg reduction rate for the female students and 90.62% egg reduction rate for the male students as shown in Table 3-9 below.

As seen in Table 3-9 below, the risk of infection with *S. mansoni* was reduced by 11.1% in females and 7.8% in males (p value <0.001).

Table 3-9: Prevalence, Cure rate (CR), Egg Reduction rate (ERR) and Risk Ratio (RR) of *S. mansoni* by gender at baseline and eight weeks after treatment

	Baseline	Eight weeks	(CR)	(ERR)	Risk Ratio	p-value	95% C.I of RR
Female	11.45%	0.8%	92.30%	93.93%	11.1%	<0.001	6.9%-17.6%
Male	12.09%	1.13%	88.46%	90.62%	7.8%	<0.001	3.1%-19.6%

As seen in Table 3-10 below, there was a significant relative reduction of the prevalence of *S. haematobium* infection for both genders. The prevalence of *S. haematobium* among girls reduced

significantly (P-value <0.001) from 20.26% to 4.3% while among the boys the infection reduced from 28.83% to 6.83%. The cure rate for *S. haematobium* was 89.13% and 87.09% among the girls and boys respectively. The egg reduction rate was 83.52% and 89.1% among the girls and boys respectively. As seen in Table 3-10 the risk of infection with *S. haematobium* was reduced by 21.23% in girls and 23.71% in boys as shown in Table 3-10 below.

Table 3-10: Prevalence, Cure rate (CR), Egg Reduction rate (ERR) and Risk Ratio (RR) of *S. haematobium* by gender at baseline and eight weeks after treatment

	Baseline	Eight weeks	CR	ERR	RR	p-value	95% C.I
Female	20.26%	4.3%	89.13%	83.52%	21.23%	0.006	7.0%- 63.9%
Male	28.83%	6.83%	87.09%	89.1%	23.71%	<0.001	16.9%-33.2%

3.3.3.2 Comparison of prevalence by age category

The prevalence of *S. mansoni* infection was reduced significantly P <0.001 among all the age-groups with the infection being substantially reduced among the >13 years old, where infection reduced from 20.0% to 0%. The cure rates ranged from 86.36% to 100% for the various age groups as shown in Table 3-11 below. The egg reduction rate was 100%, 96.05%, 84.9% and 96.10% for the 13 and above age group, 11-13, 8-10 and 5-7 age groups respectively as shown in Table 3-11 below.

In the 5-7 age groups the risk ratio of infection with *S. mansoni* was reduced by 8.85%, while in the 11-13 age group it was reduced significantly (P <0.001) by 4.8%, as seen in Table 3-11 below.

Table 3-11: Prevalence, Cure rate (CR), Egg Reduction rate (ERR) and Risk Ratio (RR) of *S. mansoni* by age group at baseline and eight weeks after treatment

	Baseline	Eight weeks later	C R	ERR	RR	p-value	95% C.I
5-7 yrs	13.20%	1.12%	92.85%	96.10%	8.85%	0.005	1.5%-46.6%
8-10 yrs	10.04%	1.64%	86.36%	84.90%	16.4%	<0.001	11.3%-23.7%
11-13 yrs	13.34%	0.06%	93.33%	96.05%	4.8%	0.004	0.6%- 38.2%
>13 yrs	20.0%	0.00%	100%	100%		<0.001	

For *S. haematobium,* infection reduced from 17.92% to 0 % this translates to 100% cure rate and 100 egg reduction rate among the 5-7 age groups. The reduction among all the age groups was significant. In the 8-10 age groups the prevalence of infection reduced from 26.48% to 8.04%, and the cure rate and egg reduction rates were 87.95% and 80.15% respectively. In the 11-13 age groups the prevalence of infection reduced from 26.78% to 5.68% with a cure rate and an egg reduction rate of 83.00% and 90.59%, respectively. However there was 0% cure rate in the 13 and above age group and the egg reduction rate was 0%, this indicates that there was no cure and no egg reduction in this age group in Table 3-12 below.

There was no risk of infection in the 5-7 age groups, this was significant as compared to other age groups where it was reduced to 30.38%, and 21.2% in the 8-10%, 11-13% age groups respectively as seen in Table 3-12 below.

Table 3-12: Prevalence, Cure rate (CR), Egg Reduction rate (ERR) and Risk Ratio (RR) of *S. haematobium* by age group at baseline and eight weeks after treatment

	Baseline	Eight weeks	Cure Rate	ERR	Risk Ratio	p-value	95% CI
5-7 yrs	17.92%	0.00%	100%	100%			
8-10 yrs	26.48%	8.04%	87.95%	80.15%	30.38%	<0.001	16.6%-55.2%
11-13 yrs	26.78%	5.68%	83.00%	90.59 %	21.2%	0.001	8.7%- 51.4%
>13 yrs	20%	20.00%	0.00%	0%	-	-	-

3.3.4 Comparison of intensities at baseline and eight weeks after treatment.

Mean intensities for both infections differ significantly. The mean intensity *S. mansoni* was at 0.65 at baseline and decreased to 0.05 after treatment while that of *S. haematobium* infection was at 1.16 at baseline and reduced to 0.15 after treatment as seen in Table 3-13 below.

Table 3-13: A comparison of mean intensities of infection at baseline and eight weeks after treatment

	Change of the mean intensity		
	Baseline	After treatment	p-value
S. mansoni	0.65±0.65	0.05±0.22	<0.001
S.haematobium	1.16±3.93	0.15±0.96	<0.001

3.3.5 Relative comparison of intensities thresholds at baseline and eight weeks after treatment

The threshold of intensities for both *S. mansoni* and *S. haematobium* infections decreased significantly. For *S. mansoni* heavy infections were eliminated during that particular period after treatment, while the risk ratio of infection with the same species was reduced by 19.78% for moderate and 5.49% for light infections, as seen in Table 3-14.

For *S. haematobium* infections the risk of infection was reduced by 11.85% for light infections and 22.92% for light infections as seen in Table 3-15.

Table 3-14: Relative comparison of *S. mansoni* intensity thresholds at baseline and eight weeks after treatment

	Baseline	Eight weeks	Risk Ratio	p-value	95% C.I
Heavy	0.22%	0.00%	Eliminated		
Moderate	3.39%	0.67%	19.78%	0.024	4.80%-80.9%
Light	8.14%	0.44%	5.49%	0.002	0.80%-34.9%

Table 3-15: Relative comparison of *S. haematobium* intensity threshold at baseline and eight weeks after treatment

	Baseline	Eight weeks	Risk Ratio	p-value	95% C.I
Heavy	7.23%	0.80%	11.85%	<0.001	9.17%-15.32%
Light	17.19%	4.72%	22.92%	<0.001	10.1%-85.6%

3.3.6 Prevalence of infection one year after treatment

The prevalence of *S. haematobium* and *S. mansoni* were 16.8% and 4.28% respectively in the period of one year after treatment as seen in Table 3-16. There was no significant difference in prevalence between sexes for both infections. There was also an increasing trend of prevalence of *S. haematobium* among the age groups as compared to prevalence before treatment, with the decrease in prevalence as the age group increases.

Further a multivariate logistic regression was done to check for any factors which would influence the infections and none of the factors (age and gender) significantly influence the infection of both *S. mansoni* and *S. haematobium*

Table 3-16: Prevalence of *S. haematobium* and *S. mansoni* one year after treatment

S. haematobium			***S. mansoni***	
Category	**Prevalence (%)**	**95%CI**	**Prevalence (%)**	**95%CI**
Overall	16.88%	13.7-21.0	4.28%	2.69-6.82
Prevalence by gender				
Male	16.84%	12.3-23.0	4.60%	2.42-8.7
Female	16.92%	12.5-23.0	3.98%	2.10-7.85
Prevalence by age groups				
5-7	24.44%	14.6- 40.9	6.67%	2.23-19.9
8-10	17.17%	12.7-23.3	2.02%	0.7-5.33
11-13	14.63%	9.74-21.9	7.3%	4.02-13.26
>13	11.76%	3.20-43.2	0.00%	0.00

3.3.6.1 Intensity of infections

The mean intensity for *S. mansoni* was 0.15 epg while for *S. haematobium* was 0.29 eggs/10ml of urine as seen in Table 3-17 below. The mean intensity among gender and different age groups are shown in Table 3-17.

Table 3-17: Geometric mean intensity of infection with *S. mansoni* and *S. haematobium* one year after treatment

Infection	Mean intensity (Geometric)±SD	95% CI	Range
S. mansoni	0.15 ±0.04	0.08-0.24	0-145
Gender			
Female	0.5±0.05	0.04-0.26	1-145
Male	0.16±0.06	0.05-0.28	1-73
Age group			
5-7	0.23±0.17	0.00-0.58	1-25
8-10	0.07±0.040	0.00-0.15	1-145
11-13	0.28±0.10	0.10-0.48	1-73
>13 yrs	0±0	0.00-0.00	1-0
S. haematobium	0.29 ±0.05	0.19-0.39	0-1001
Gender			
Female	0.29±0.76	0.15-0.44	1-211
Male	0.29±0.76	0.15-0.44	1-1001
Age group			
5-7	0.45±0.23	0.09-0.92	1-217
8-10	0.31±0.86	0.1-0.48	1-1001
11-13	0.23±0.07	0.09-0.38	1-205
>13 yrs	0.08±0.14	0.00-0.22	1-2

Intensity threshold

As can be seen in Table 3-18 below the heavy intensity threshold for *S. mansoni* and the moderate intensity threshold for *S. haematobium* were reduced to 0%. It is worth noting that the threshold of heavy infections for *S. haematobium* stands at 1.70%. The threshold of light infections with *S. haematobium* was significantly higher at 15.15%, as compared to *S. mansoni* at 4.03%.

Table 3-18: Intensity threshold of *S. mansoni* and *S. haematobium* one year after treatment

	S. mansoni		***S. haematobium***	
	Prevalence	95% CI	Prevalence	95% CI
Heavy	0.00%		1.70%	0.03%-8.32%
Moderate	0.25%	0.03%-1.79%		
Light	4.03%	1.9%-8.26%	15.15%	13.74%-16.51%

3.3.7 Dual infection

The overall prevalence of dual infections with both *S. mansoni* and *S. haematobium* was 1.55% (95% CI 0.6%-3.69%) as seen in Table 3-19.

Further a multivariate logistic regression was done to check for any factors which would influence the dual infection and none of the factors (age, sexes) significantly influenced the infection of both *S. mansoni* and *S. haematobium*.

Table 3-19: Prevalence of Dual infection one year after treatment

Category	Prevalence	95% CI
Overall	1.55%	0.6%-3.69%
Prevalence by gender		
Female	1.22%	0.3%-4.86%
Male	1.8%	0.6%-5.75%
Age category		
5-7 yrs	3.03%	0.44%-20.86%
8-10 yrs	1.22%	0.31%-4.83%
11-13 yrs	1.80%	0.45%-7.11%
>13 yrs	0.00%	

3.3.8 Comparison of Prevalence at Baseline and one year after treatment

Overall relative comparison of prevalence between the baseline and one year after treatment was done as seen in Table 3-20 below. In both infections there was a significant reduction of prevalence. The prevalence of *S. mansoni* reduced from 11.76 % at baseline to 4.28%, while that of *S. haematobium* reduced from 24.43% to 16.88% in the period of one year of treatment. The reduction in prevalence in the period of one year after treatment was 67.30% and 37.96% for

S. mansoni and *S. haematobium* respectively. The egg reduction rate was 76.92% and 75% for *S. mansoni* and *S. haematobium* respectively.

The risk of infection with *S. mansoni* reduced by 36.38% , while that of *S. haematobium* reduced by 69.06% in the same time period after treatment, as seen in Table 3-20 below.

Table 3-20: Prevalence Egg Reduction Rate (ERR) and Risk Ratio (RR) of *S. mansoni* and *S. haematobium* at baseline and one year after treatment.

	Baseline	One year later	ERR	Risk Ratio	p-value	95% C.I of the Risk ratio
S. mansoni	11.76%	4.28%	76.92%	36.38%	<0.001	26.0%-50.1%
S. haematobium	24.43%	16.88%	75.00%	69.06%	<0.001	57.9%-82.4%

3.3.8.1 Absolute comparison of prevalence by gender

There was significant reduction in prevalence by gender in *S. mansoni* infections, the prevalence of infection reduced to 3.98% from 11.45% and to 4.60 from 12.09% for girls and boys respectively as seen in Table 3-21 below.

The reduction in prevalence in the period of one year after treatment was 69.23% and 65.38% for the girls and boys respectively. The egg reduction rate was 24.24% and 75.00% for the girls and boys respectively as shown in Table 3-21.

There was significant reduction in prevalence of *S. mansoni* infections by gender for both boys and girls, the risk ratio for infection reduced to34.74% for girls and to 37.97% for boys as seen in Table 3-21.

Table 3-21: Prevalence, Egg Reduction Rate (ERR) and Risk Ratio (RR) by gender of *S. mansoni*, before and one year after treatment

	Baseline	One year	ERR	RR	p-value	95% C.I
Female	11.45%	3.98%	24.24%	34.74%	<0.001	19.17%-63.0%
Male	12.09%	4.60%	75.00%	37.97%	<0.001	20.4%-70.7%

There was no significant reduction of infection for *S. haematobium* among the girls, where prevalence was at 20.26% at baseline and at 16.91% one year after treatment. In the boys there was significant reduction in prevalence from 28.83% at baseline to 16.83% one year later after treatment.

The reduction in prevalence in the period of one year after treatment was 26.08% and 46.77% for the girls and boys and respectively. The egg reduction rate was 65.88% and 81.16% for the female and male students respectively as seen in Table 3-22 below.

The risk ratio for infection reduced by 83.47% for girls and by 58.39% for boys as seen in Table 3- 22.

Table 3-22: Prevalence, Egg Reduction Rate (ERR) and Risk Ratio (RR) of *S. haematobium* by gender at baseline and one year after treatment

	Baseline	One year	E R R	R R	p-value	95% C.I
Female	20.26%	16.91%	65.88%	83.47%	0.391	Not significant
Male	28.83%	16.83%	81.16%	58.39%	0.002	41.7%-81.7%

3.3.8.2 Comparison of prevalence by age category

Comparing the prevalence of infection for *S. mansoni* shows that the prevalence of infection after one year of treatment for the 13 years and above year's age group was completely eliminated at that period after treatment, and therefore the risk was also eliminated at that age group. The prevalence of *S. mansoni* reduced significantly in the 8-10 years age groups as seen in Table 3-23.

The Reduction in prevalence for the age groups of 5-7, 8-10, 11-13 and over 13 years was 78.57%, 81.81%, 33.33%, and 100% respectively.

The egg reduction rate for the age groups of 5-7, 8-10, 11-13 and over 13 years was 70.13%, 86.79%, 63.15%, and 100 respectively as seen in Table 3-23.

The prevalence of *S. mansoni* reduced significantly in the 8-10 age groups, with the risk of infection being reduced by 20.11%, as seen in Table 3-23.

Table 3-23: Prevalence Egg Reduction Rate (ERR), and Risk Ratio (RR) of *S. mansoni* by age group at baseline and one year after treatment.

	Baseline	One year	ER R	Risk Ratio	p-value	95% C.I
5-7 yrs	13.20%	6.67%	70.13%	50.47%	0.005	1.5%-46.6%
8-10 yrs	10.04%	2.02%	86.79%	20.11%	<0.001	11.3%-23.7%
11-13 yrs	13.34%	7.3%	63.15%	50.50%	0.004	0.6%-38.2%
>13 yrs	20.0%	0.00%	100%	0%		

For *S. haematobium* there were re - infections and new infections in the 5-7 age group, whereby prevalence of infection with the same species was at 17.92% at baseline and 24.4% one year later after treatment.

The reduction in prevalence for the age groups of 5-7, 8-10, 11-13 and over 13 years was 45.12%, 76.33%, 81.88%, and 66.60% respectively

There was a significant egg reduction rate across the age groups 5-7, 8-10, 11-13 and over 13 years which were at 45.12%, 76.13%, 81.88%, and 66.60% respectively as seen in Table 3-24.

The risk for infection reduced slightly across the age groups, as seen in Table 3-24.

Table 3-24: Prevalence, Egg Reduction Rate (ERR) and Risk Ratio (RR) of *S. haematobium* by age group at baseline and one year after treatment

	Baseline	One year	ERR	RR	p-value	95% CI
5-7 yrs	17.92%	24.4%	45.12%	Re-infections		
8-10 yrs	26.48%	17.17%	76.33%	64.83%	0.011	16.6%-55.2%
11-13 yrs	26.78%	14.59%	81.88%	54.5%	<0.001	8.7%-51.4%
>13 yrs	20%	11.76%	66.60%	58.82%	0.475	Not significant

3.3.8.3 Comparison of intensities at baseline and one year after treatment.

Mean intensities for both infections differ significantly. The mean intensity *S. mansoni* was at 0.65 epg at baseline and reduced to 0.15 epg in a period of one year after treatment while that of *S. haematobium* infection was at 1.16 egg/ 10ml of urine at baseline and reduced to 0.29 eggs/10ml of urine epg in a period of one year after treatment as seen in Table 3-25 below.

Table 3-25: A comparison of mean intensities of infection one year after treatment

	Change of the mean intensity		
	Baseline	1 year after treatment	p-value
S. mansoni	0.65 ±0.65	0.15 ±0.19	<0.001
S. haematobium	1.16 ±3.93	0.29 ±1.23	<0.001

3.3.8.4 Relative comparison of intensities at baseline and one year after treatment

The threshold of intensities for both *S. mansoni* and *S. haematobium* infections decreased significantly. For *S. mansoni* heavy infections were eliminated within a period of one year after treatment, while the risk ratio of infection with the same species was reduced by 7.42% for moderate and 49.48% for light infections, as seen in Table 3-26 below.

For *S. haematobium* infections the risk of infection was reduced within a time period of one year after treatment by 1.70% for heavy infections and 15.15% for light infections as seen in Table 3-27 below.

Table 3-26: Intensity threshold and Risk Ratio of *S. mansoni* at baseline and one year after treatment

	Baseline	One year after treatment	Risk Ratio	p-value	95% C.I
Heavy	0.22%	0.00%	Eliminated		
Moderate	3.39%	0.25%	7.42%	0.008	1.09%-50.2%
Light	8.14%	4.03%	49.48%	0.002	3.72%-77.19%

Table 3-27: Intensity threshold and Risk Ratio of *S. mansoni* at baseline and one year after treatment

	Baseline	One year after treatment	Risk Ratio	p-value	95% C.I
Heavy	7.23%	1.70%	24.35%	0.061	Not significant
Light	17.19%	15.15%	87.8%	0.225	Not significant

3.3.8.5 Summary of prevalences

The Tables below i.e. 3-28, 3-29 and 3- 30, summarize the infection prevalences of *S. mansoni* and *S. haematobium* as well as dual infections in the periods before treatment, eight weeks after treatment and one year later.

Table 3-28: Prevalence of *S. haematobium* at different stages of the study period and comparison of the prevalence by gender and age.

	Before Treatment		**Eight weeks after treatment**		**One year after treatment**	
	Prevalence	**95%CI**	**Prevalence**	**95% CI**	**Prevalence**	**95% CI**
S. haematobium						
Overall	24.43%	20.4-28.4	5.58%	2.63-8.53	16.87%	13.7-21.0
Female	20.26%	15.0-25.5	4.31%	0.61-8.00	16.91%	12.5-23.0
Male	28.83%	22.7-34.9	6.83%	2.26-11.41	16.83%	12.3-23.0
5-7yrs	17.92%	10.6-25.2	0.00%		24.4%	14.6- 40.9
8-10yrs	26.48%	20.6-32.3	8.04%	2.33-13.76	17.17%	12.7-23.3
11-13 yrs	26.78%	18.6-34.9	5.68%	0.84-10.52	14.59%	9.74-21.9
>13 yrs	20%	0.0-55.1	20.00%	0.0-22.18	11.76%	3.20-43.2

Table 3-29: Prevalence of *S. mansoni* at different stages of the study period and comparison of the prevalence by gender and age.

	Before Treatment		Eight weeks after treatment		One year after treatment	
	Prevalence	**95%CI**	**Prevalence**	**95% CI**	**Prevalence**	**95% CI**
S. mansoni						
Overall	11.76%	8.7-14.8	1.12%	0-2.28	4.28%	2.69-6.82
Female	11.45%	7.3-15.5	0.8%	0-2.13	3.98%	2.10-7.85
Male	12.09%	7.7-16.5	1.33%	0-2.84	4.59%	2.42-8.7
5-7yrs	13.20%	6.7-19.6	1.12%	0-3.31	6.67%	2.23-19.9
8-10yrs	10.04%	6.1-14.0	1.64%	0-3.59	2.02%	0.7-5.33
11-13 yrs	13.39%	7.1-19.7	0.06%	0-0.91	7.34%	4.02-13.26
>13 yrs	20.00%	0.0-55.1	0.00%		0.00%	

Table 3-30: Prevalence of Dual infections at different stages of the study period and comparison of the prevalence by gender and age.

	Before Treatment		Eight weeks after treatment		One year after treatment	
	Prevalence	**95%CI**	**Prevalence**	**95% CI**	**Prevalence**	**95% CI**
Dual infection						
Overall	5.43%	3.6-8.0%	0.00%	0.00%	1.55%	0.6%
Female	5.72%	3.3-9.1%	0.00%	0.00%	1.22%	0.30-4.86
Male	5.11%	2.8-9.0%	0.00%	0.00%	1.80%	0.60-5.75
5-7yrs	6.60%	3.2-13.5%	0.00%	0.00%	3.03%	0.44-20.9
8-10yrs	5.93%	3.5-10.5%	0.00%	0.00%	1.22%	0.31-4.83
11-13 yrs	3.57%	1.3-9.3%	0.00%	0.00%	1.80%	0.45-7.11
>13 yrs	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%

3.3.9 Prevalence of soil transmitted helminthes

The infections for STH were minor in terms of prevalence and too low for adequate statistical analysis, but have been reported in Table 31 below. The overall prevalence of hookworm, Ascaris and Trichuris in the period before treatment, eight weeks and one year after treatment was below 1%. The prevalence among the sexes was below 1%. Among the different age groups, the prevalence was 1.34% in the 11-13 years age group, while for the other age groups it was below 1% as seen in Table 3-31

Table 3-31: Prevalence of STH infections at different stages of the study period and comparison of the prevalence by gender and age.

	Before Treatment			Eight weeks after treatment			One year after treatment		
STH Infections									
	Prevalence			Prevalence			Prevalence		
	Hookworm	Ascaris	Trichuris	Hookworm	Ascaris	Trichuris	Hookworm	Ascaris	Trichuris
Over all	0.90%	0.27%	0.45%	0.89%	0.22%	0.45%	0.00%	0.00%	0.75%
Male	0.68%	0.00%	0.45%	0.67%	0.00%	0.45%	0.00%	0.00%	0.25%
Female	0.22%	0.22%	0.00%	0.89%	0.22%	0.00%	0.00%	0.00%	0.44%
5-7yrs	0%	0.22%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.44%
8-10yrs	0.22	0.00%	0.45%	0.22%	0.00%	0.22%	0.00%	0.00%	0.25%
11-13yrs	0.45%	0.00%	0.00%	1.34%	0.22%	0.22%	0.00%	0.00%	0.00%
>13 yrs	0.22%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%

3.4 The IgE profile in the school going children infected with schistosomiasis at baseline and after treatment.

3.4.1 General view of IgE levels at baseline and after treatment

The nonparametric Wilcoxon sum rank tests (Mann-Whitney *U* tests) for the independent samples were performed to compare before and after treatment antibody- antigen reaction optical densities (ODs). A quartile regression was performed to check the relationship of the optical densities and age. The test was conducted for two antigens namely SEA and SWAP. All statistical analyses were conducted in STATA 12 and *P* values of <0.05 were considered significant.

From Table 3-32 below it is evident that the change in OD level of IgE were higher before treatment as compared to after treatment of the primary school children. The mean IgE OD values for SEA was 0.128 before treatment and 0.073 after treatment.

Table 3-32: Summary statistics of IgE values at baseline and eight weeks after treatment, for SEA and SWAP

	SEA		**SWAP**	
	Before treatment	After treatment	Before treatment	After treatment
Min	0.0415	0.041	0.04075	0.038
Median	0.0685	0.61	0.05975	0.58
Mean	0.128	0.073	0.0651	0.0719
Standard deviation	0.106	0.059	0.0265	0.063
Skew	1.351	4.8	7.36	5.011
Maximum	0.5945	0.49	0.4155	0.51

3.4.2 Comparison of IgE levels at baseline and after treatment

Out of the (49/442) infected with *S. mansoni* before treatment only five were infected after treatment. The cases were positive for *S. mansoni* before treatment and after treatment. The children recorded IgE OD levels of 0.0833 and 0.0674 in the period before treatment and after treatment with praziquantel respectively as seen in Table 3-33 below. The reduction in IgE level was significant.

Table 3-33: IgE levels for positive *S. mansoni* individuals at baseline and after treatment

	Before treatment	**After treatment**	**H_a mean(B.T>A.T)**
SEA	**0.0833±0.065**	**0.0674±0.026**	**p-value =0.0423**
SWAP	0.0638±0.026	0.0652±0.017	p-value=0.3775

***Ha-** Alternative hypothesis

***B.T** –Mean before treatment

***A.T-** Mean after treatment

Where **Ha: B.T>A.T** Mean before treatment should be greater than mean after treatment

Out of (103/442) children infected with *S. haematobium* 57 were followed up. Four of the followed up children reported infections after treatment and they recorded the following ODs. Higher IgE level were recorded in the four children that tested positive for *S. haematobium* eight weeks after treatment with praziquantel. As seen in Table 3-34 the IgE OD level was 0.176 and 0.072 in the period before treatment and after treatment respectively

Table 3-34: IgE levels for positive *S. haematobium* individuals at baseline and after treatment

	Before treatment	**After treatment**	**H_a mean(B.T>A.T)**
SEA	**0.1766±0.119**	**0.072±0.054**	**p-value =0.0000**
SWAP	0.0600±0.116	0.070±0.062	p-value=0.2365

***Ha-** Alternative hypothesis

***B.T** –Mean before treatment

***A.T-** Mean after treatment

Where **Ha: B.T>A.T** Mean before treatment should be greater than mean after treatment

None of the children who had dual infection before treatment tested positive for either *S. mansoni* or *S. haematobium*. The IgE levels showed a remarkable decrease, the mean IgE titers decreased significantly ($p<0.0001$) from 0.118 ± 0.098 to 0.068± 0.002 for SEA while for SWAP there was an increase in the period after treatment 0.52 ±0.00408 to 0.064±0.0122.

3.5 Relationship between IgE antibody level with age among the primary school children infected with schistosomiasis

3.5.1 IgE profiles in relation to gender and Age

The overall IgE profile against SEA antigen was significantly higher before treatment as compared to after treatment. As seen in Table 3-35 below, the mean IgE OD level was 0.128 before treatment and 0.073 after treatment with praziquantel.

When comparing with gender, there was not so much significant difference observed in the IgE levels. For the female pupils, the IgE OD level was 0.133 before treatment and 0.079 after treatment with praziquantel, while for the male pupils it was 0.123 and 0.066 respectively.

In terms of age there was significant change in the IgE levels, across all age groups, levels decreases significantly after treatment as seen in Table 3-35 below. In the period after treatment the IgE OD levels increased from 0.063 at age group 5-7 years to 0.091 at age group 11-13 years.

Table 3-35: IgE levels against SEA displayed across gender and age.

	Before treatment (mean±SEM)	**After treatment (mean±SEM)**	**Z an P values**
Overall 442	**0.128±0.106**	**0.073±0.059**	**Z=6.56, p=0.0000**
Gender			
Female 215	**0.133±0.108**	**0.079±0.0075**	**Z=5.61,P=0.000**
Male 227	**0.123±0.103**	**0.066±0.340**	**Z=3.54,P=0.0004**
Age categories			
5-7yrs 106	**0.124±0.116**	**0.063±0.033**	**Z=2.65,P=0.008**
8-10yrs 219	**0.134±0.106**	**0.070±0.049**	**Z=5.71,P=0.0000**
11-13yrs 112	0.121±0.094	0.091±0.091	Z=1.96, P=0.0496
>13yrs 5	0.127±0.094	0.058±0.013	Z=0.94,P=0.3472

The overall IgE profile against SWAP antigen was higher after treatment as compared to before treatment. As seen in Table 3-36 below, the mean IgE OD level was of 0.065 before treatment and 0.071 after treatment with praziquantel.

When comparing with gender, there was significant difference observed in the IgE levels. For the female pupils, the IgE OD level was 0.064 before treatment and 0.078 after treatment with praziquantel. For the male pupils it reduced slightly, where it was 0.065 before treatment and 0.064 after treatment respectively.

In terms of age there was change in the IgE levels. In most of the age groups, levels increased slightly after treatment as seen in Table 3-36 below. In the period after treatment the IgE values decreased from OD of 0.070 at age group 5-7 years to 0.067 at age group 11-13 years.

Table 3-36: IgE levels against SWAP displayed across gender and age.

	Before treatment (mean ±SEM)	**After treatment (mean ±SEM)**	**Z and P**
Overall	**0.065±0.0265**	**0.071±0.063**	**Z=3.26,P=0.0011**
Gender			
Female	**0.064±0.020**	**0.078±0.083**	**Z=2.87,P=0.0004**
Male	**0.065±0.031**	**0.064±0.028**	**Z=1.69,P=0.09**
Age categories			
5-7yrs	**0.070±0.045**	**0.067±0.059**	**Z=3.34,P=0.0008**
8-10yrs	**0.062±0.015**	**0.070±0.062**	**Z=2.06,P=0.0389**
11-13yrs	**0.065±0.015**	**0.080±0.073**	Z=0.43,P=0.6671
>13yrs	**0.058±0.020**	**0.065±0.012**	Z=0.94,P=0.3472

3.5.2 Quartile regression of IgE in relation to age

A quartile regression analysis was performed to study further the relationship between IgE and age. It was observed that there was an increase in IgE level with age as seen in Table 3-37 below. The IgE OD level increased by 0.000875 against SEA for every additional increase in the age of the children and the relationship is significant (P- 0.015) after the treatment.

Likewise for SWAP antigen, there as an increase in IgE level with age in the period after treatment with praziquantel. As seen in Table 3-37 there was a significant (P 0.034) increase in IgE level against SWAP, which increased by 0.001 units for every additional one year increase in age of the children after treatment.

Table 3-37: Quartile regression of IgE in relation to age.

IgE	**Age(co-efficient and p-values)**	
	Before treatment	After treatment
SEA	0.000375(p-value=0.792)	**0.000875(p =0.015)**
SWAP	0.00025(p-value=0.541)	**0.001(p =0.034)**

.

CHAPTER 4

DISCUSSION

4.1 The infection status of STH and schistosomiasis in the school going children.

The current study reveals that STH are not prevalent in the study area. The very low prevalences (>1%), indicate that there is a high cure rate of STH after annual deworming in the area. There is also an indication of low transmission intensity of the same. Regular deworming and high standards of hygiene can drastically reduce previously high infection rates of STH (WHO 2003). It is worth noting that the schools were well supplied with piped water and the toilets had cemented floors, these are some of the factors that could have contributed to low prevalence rates of STH.

The current study reveals that indeed both *S. mansoni* and *S. haematobium* are still prevalent in Taveta region with that of *S. haematobium* being higher, compared to that of *S. mansoni*. Similar infection situations have been observed in different geographical areas in Kenya (Siongok *et al.,* 1976; Butterworth *et al.,* 1991; Odiere *et al.,* 2012; Masaku *et al.,* 2015). The intensities of *S. mansoni* and *S. haematobium* are quite low in this study. The reduction in egg intensities could well be attributed to the annual national deworming programme which had been going on for 2 years before data was collected for this study.

Despite the annual national deworming programme in Kenya, the prevalence rates observed in Taveta are of public health importance. A study conducted in neighboring Tanzania in 2012, revealed a pretty much similar situation, 360 school children (aged 6–17 years) were parasitologically examined; 62 % and 57.7% of males and female were infected with *S. mansoni* respectively. Evidence revealed in the study indicates that despite considerable efforts made to control schistosomiasis in Tanzania, the disease remains a serious public health problem and its

prevalence continues to increase with increase in the population size (Mazigo *et al.,* 2012). A similar situation has been observed in Yemen, where the prevalence rate of schistosomiasis among children in rural Yemen was 31.8%. This prevalence is considered to be high since the children were under a control programme (Sady *et al.,* 2013).

In terms of Location, the data on prevalence of infection was collected from four primary schools, in slightly different geographical locations in Taveta region. The children in Abori, Lotima and Eldoro primary schools were more likely to be infected with *S. mansoni* as compared to Children in Kiwalwa Primary school (OR 1.03,1.11, 1.02) respectively. This finding can be attributed to the fact that Kiwalwa primary school is located in a more urban setting, in Taveta town as compared to the other 3 schools that are interior to the town whose settings are rural, with Lotima primary being furthest from the town at the Kenya Tanzania border. Children in town/urban settings are different in terms of dressing and practices. Children in urban areas are highly likely put on shoes compared to children in rural area, and this relates to a reduction in transmission of infection. Children in urban areas are also less likely to be involved in household chores like fetching of water or farming from rivers or canals that are infected with cercariae, as compared to children in rural settings where these chores are a norm. Children in urban settings have the privilege of piped water, and most agricultural practices are usually found in the rural setting as compared to urban settings that are more industrialized and less agricultural in terms of economic activities.

In terms of prevalence with age this current study indicates that the age group of 11-13 years had a high prevalence of *S. haematobium* at (26.8%), followed closely by the 8-10 years at (26.5 %). The prevalence of *S. mansoni* was highest among the age of > 13 years at (20%) while that of 11-13 years was at (13.4%). This study reveals that prevalence of infection for both *S. mansoni* and *S. haematobium* peak at ages 8-13 years then gradually decrease. A study conducted 36 years ago in three villages in Taveta, reveals a parallel situation to this current study that children display the

highest rate of infection with schistosomiasis. The study further revealed that egg positive rate increase rapidly with age in children and reach a peak between the ages of 5-14years then gradually decrease (Katamine *et al.,* 1978). In the current study Primary school age children have served as an indicator of the infection status in Taveta population. A prevalence study conducted in Brazil revealed the advantage of conducting schistosomiasis prevalence survey using primary school age children (Pereira *et al.,* 2010). The age group of children aged 6-15 years, serves as a tool for comparative analysis of prevalence in that infection prevalence in this age group demonstrated the highest positive correlation with overall population prevalence. This age group is useful both as a target group and a reference point as it is the age range established for formal schooling in Kenya and many developing countries where schistosomiasis is endemic.

In this study the prevalence was higher in boys as compared to girls where prevalence of *S. haematobium* was significantly higher in the male children as compared to the female children (28.8% vs. 20.3%, P-0.03). It was observed that the female children were significantly less likely to be infected with *S. haematobium* compared to male (OR-0.4896, p-value 0.031). This corresponds to a study in Nigeria where the results showed that the males were generally more infected and with higher intensity than the females (Uneke *et al.,* 2006). This observation can be attributed to the fact that male pupils have higher water contact activities. It is also worth noting that other common water contact activities including playing, swimming, fishing, wading and bathing in cercariae infested water bodies are male dominated, whereas girls are more conservative especially when it comes to swimming in open water bodies as compared to boys. It is worth noting that although females are less likely to get infected, as compared to boys, they are also exposed as they are responsible for chores like fetching water and washing clothes and utensils at these water sources.

The prevalence of infection in this study indicates that despite annual treatment, transmission intensities are high; therefore the infection status of *S. mansoni* and *S. haematobium* remains endemic. Worth noting is that the prevalence rate of *S. mansoni* in this study was higher than those reported Nigeria (4.6%) (Goselle et al., 2010) Ethiopia (5.95 %) (Dejenie et al., 2010) and 2.1 %) (Yami *et al.,* 2011). The difference could be due to the study period and the method of laboratory diagnosis employed as previously described (Bajiro *et al.,* 2016b). However, there are studies that report prevalences higher than those found in this study. These reports include: Brazil (14.4 %), Nigeria (12.6 %), Ghana (19.8%), Uganda (27.8 %), Northwestern Tanzania (64.3 %), southern Tigray (73.9 %), Gonder (89.9 %), Jimma Zone (24.0 %.), Wondo Genet (74.9 %), Wollega (67.6 %), Tumuga (63.3%) and Waja (73.84%) from Ethiopia, Yemen (31%), Egypt (31.4%) (Alemu *et al.,* 2011; Anto *et al.,* 2013; Bajiro *et al.,* 2016b; Dejenie *et al.,* 2010; Goselle *et al.,* 2010; John *et al.,* 2008; Ojurongbe *et al.,* 2014; Traore *et al.,* 1998; Worku *et al.,* 2014). The difference might be due to long time endemicity of the parasite in these study areas, the study design employed and ecological differences as previously described (Bajiro *et al.,* 2016b). On the other hand, in the case of *S. haematobium*, the prevalence in this study was lower than that in Ghana (33.2%), Nigeria (37%, 53.1%, 70.0% and 46.18%), Mali (55.2%) and Senegal (73.2 % and 57.7%) and Zimbabwe (21.0 %) (Anto *et al.,* 2013; Banji *et al.,* 2012; Mutapi *et al.,* 2011; Ojurongbe *et al.,* 2014; Oniya & Jeje, 2010; Ozwara *et al.,* 2011; Senghor *et al.,* 2015, 2016; Traore *et al.,* 1998). Perhaps the factors previously described above regarding higher prevalence rates in other studies from other regions as compared to the prevalence from this study could be the reason for this comparatively lower prevalence rate. Some of these reasons may be due to either long time endemicity of the parasite in these other studies areas than the current feature of our study area, the study design employed and ecological differences as previously described (Bajiro *et al.,* 2016b). However, the frequency of contact with water sources in the form of habitual practices could have been a contributing factor to a higher prevalence rate than that in

this study. Moreover, it has also been suggested that a direct correlation between water contact activities and transmission of schistosomiasis could result in higher prevalence rates (Anto *et al.,* 2013). Therefore, it could be concluded that comparatively, the prevalence of *S. haematobium* in this study in relation to these other studies was lower because of a significant decrease in water contact activities in this region. However, prevalence of *S. haematobium* in this study is higher than that recorded in Yemen (18.6%) and Ipogun in Nigeria (18%) and Pemba Island (18.9%) (Abdulrab *et al.,* 2013; Guidi *et al.,* 2010; Oniya, *et al.,* 2013).

In terms of dual infection, analysis revealed that out of the 442 primary school children 24 had dual infection (both *S. mansoni* and *S. haematobium).* A study conducted in 2008 in Taveta among 470 primary school children revealed 44% infection rate by either *S. mansoni, S. haematobium* or with both species, co-infection (Gouvras *et al.,* 2013). As for the children with dual infection this study revealed infection rates did not differ significantly with sexes. The dual infection status was at 5.11% for the boys, while for girls it was 5.72%. While the infection did not differ significantly among the age groups, the 5-7yrs age group had the highest percentage prevalence of dual infections followed by the 8-10 age groups. Worth noting is that the age group of 13 years and above did not have a single case of dual infections. In spite of these findings, a multivariate logistic regression statistical test that checked on the influence of age and gender on dual infections, found that none of these factors significantly influenced dual infections.

With regards to dual infection prevalence rates, there seems to be an inadequacy of data from schistosomiasis prevalence studies. This is despite the high overall prevalences of both *S. mansoni* and *S. haematobium* being noted in certain studies such as that from Ghana (47.7%) (Anto *et al.,* 2013). In this study the prevalence of dual infection indicates that transmission of both intestinal and urinary schistosomiasis is common. This represents a serious health situation given that each

infection has got its own pathology therefore double morbidity, which results in a double burden for an infected child.

4.2 The efficacy of treatment of single and dual *Schistosoma mansoni* and *Schistosoma haematobium* infection in the school going children at eight weeks and one year after treatment.

In this present study, the prevalence of *S. mansoni* reduced from 11.76% to 1.12% while that of *S. haematobium* reduced from 24.43% to 5.58% and dual infections were significantly reduced in the period of 8 weeks after treatment. In both infections the reduction in prevalence was highly significant. The geometric mean intensities of both infections decreased, with a significant difference being observed *S. mansoni*. The threshold of intensities equally decreased, the heavy infections for *S. mansoni* were not observed after treatment, consequently reducing the risk of infection by 0% with the species in the period of eight weeks after treatment. The intensity threshold for heavy infections with *S. haematobium* equally reduced from 7.23% to a negligible 0.80%. The therapeutic efficacy of PZQ at 40mg/Kg body weight against *S. mansoni* and *S. haematobium* translated to high cure rates of 90.38%, with ERR of 92.31% and 87.9%, ERR of 87.06% respectively. Treatment with Praziquantel in this study can be considered as highly efficacious as it reduced the risk of infection with *S. mansoni* to a significant 9.5% while that of *S. haematobium* reduced to 22.38%.

In this current study the efficacy of PZQ at 40mg/Kg body weight against *S. mansoni* had a higher efficacy when compared with findings from Waja (CR = 88.99%) (Dejenie *et al.,* 2010) and Finchaa valley (CR = 80.9% and ERR = 99.51%) (Haile *et al.,* 2012) from Ethiopia and from Egypt (CR = 62.5%) (Botros *et al.,* 2005). This could be explained in part by differences due to baseline infection intensity, duration of post-treatment, presence of immature stages of the

parasite (Bajiro *et al.,* 2016). However, the efficacy of PZQ in this current study is almost comparable to that from Timuga (CR = 93.44%) from Ethiopia (Dejenie *et al.,* 2010).

In comparison to a study conducted among primary school children in Kangundo, Kenya, the efficacy is as well much similar to the one in this study. Results of the Kangundo study show a CR of 87.2 in the case of 8 weeks post-treatment (Thiongo et al., 2002). There is however a study with an efficacy higher that that reported in this study from Jimma Zone, Ethiopia (CR = 99.1% and ERR = 99.9%) (Bajiro *et al.,* 2016). One significant reason for this difference could be the post-treatment length with that of Jimma Zone (Bajiro *et al.,* 2016) being 21 days as opposed to 8 weeks in the case of this study.

With regard to *S. haematobium*, the efficacy of PZQ at 40mg/Kg body weight in this study was almost comparable to that of Nigeria (CR = 85.5% and ERR = 77.6%) (Ojurongbe *et al.,* 2014) at 8 weeks post-treatment and Senegal (CR = 89.4% and ERR = 77.6%) (Senghor *et al.,* 2015). However, this efficacy is lower than that from findings in Senegal (CR = 92.9%) (Senghor *et al.,* 2016), Pemba (CR = 95) at 7 weeks post-treatment (Guidi *et al.,* 2010), Zimbabwe (CR = 92% and ERR = 99%) (Mutapi *et al.,* 2011), and Nigeria (CR = 94.44%) (Oniya & Jeje, 2010). Moreover, another study in Kenya, in 1990, reported a higher efficacy that that from our study at the same dosage of 40mg/Kg (CR = 96%) (King *et al.,* 2000). However, the efficacy registered in Kenya in 1986 was as well comparatively lower than that in this study (CR = 65%).

Although this study reported high cure rate and egg reduction rates, there was a case of negative egg reduction in the period of eight weeks after treatment. This is an indication of increase in geometric mean, and therefore this further indicates that there was a case of re-infection shortly after treatment. A study conducted among school children in Nigeria, demonstrated the efficacy of two doses of Praziquantel for the treatment of urinary schistosomiasis. The study revealed that

positive children aged 4-15 with *S. haematobium* infection who received a single dose of 40mg/kg twice with a four week interval had high ERR of 77.6% and 100% (Ojurongbe *et al.,* 2014).

In an attempt to explanation for low egg reduction rates some studies have identified that patients in high transmission areas harbor high numbers of immature schistosomes are less susceptible to Praziquantel (Keiser *et al.,* 2009, Erko *et al.,* 2012). These immature schistosomes have high chances of surviving a single dose of Praziquantel treatment in a year.

Past studies have reported a high efficacy of Praziquantel when administered as two or three treatments spaced at different but close time intervals (Guisse *et al.,* 1997; Liang *et al.,* 2000; de silva *et al.,* 2005; Olds *et al.,* 1999, Kabatereine *et al.,* 2003)

There was a significant reduction in prevalence of *S. mansoni* infection for both sexes. It is worth noting though that the reduction in prevalence was higher among the female pupils from 11.42% to 0.8% as compared to the male pupils 12.09% to 1.13%. This translates to a greater reduction in the risk of infection among the female pupils at 7.8% as compared to the male pupils at 11.1%. Equally the cure rate and egg reduction rates were higher among the female pupils compared to the male pupils. Though slight, differences in reduction of prevalence, cure rate and risk ratio were also noted among pupils infected with *S. haematobium,* and just like in *S. mansoni,* girls recorded higher cure rates and less risk of infection with the species. The prevalence of *S. haematobium* among the girls and boys reduced significantly with greater reduction being observed among the girls as compared to the boys. The differences in higher prevalences after treatment, lower cure rates and higher risk ratio among gender can be attributed to factors described previously whereby boys are more predisposed to infection as compared to the girls

Prevalences among the age groups decreased significantly with infection of *S. haematobium* being greatly reduced at age group 5-7 years where it reduced from 17.92% to 0% translating to a cure

rate and an egg reduction rate of 100%. This indicates that there was no risk of infection for this age group with the species in the period eight weeks after treatment.

The prevalence of *S. mansoni* was equally significantly reduced in the 13 and above age group, where infection reduced from 20% to 0%, translating to a cure rate and egg reduction rate of 100%. This eradicates the risk of infection for that species in the period eight weeks after treatment. It is worth noting that in the 11-13 age group risk of infection was significantly reduced by 4.8% while that of the 5-7 age groups was reduced by 8.85% in the period of eight weeks after treatment.

In the period one year after treatment the prevalence of *S. haematobium* and *S. mansoni* were 16.8% and 4.28% respectively. This translates to an increase compared to the period of eight weeks after treatment, signifying reinfection. On the contrary there was a significant reduction in prevalence, *S. mansoni* reduced from 11.76% at baseline to 4.28%, while that of *S. haematobium* reduced from 24.43% to 16.88% in the period of one year after treatment.

There was significant reduction in prevalence by gender in *S. mansoni* infections, the prevalence reduced to 3.98% from 11.45% and from to 4.60% from 12.09% for girls and boys respectively. In terms of age the prevalence of infection with the same species was completely eliminated for the 13 years and above age group in the period of one year after treatment, equally eliminating the risk of infection

For *S. haematobium* the prevalence of infection in the 5-7 age groups was at 17.92% at baseline and 24.4% one year after treatment. The mean intensities and the egg reduction rates were minimal across the age groups with the lowest being at the age group of 13 and above. This signifies that there were re infections and new infections in the period of one year after treatment.

One year reduction in prevalence of this study was comparatively lower than all the prevalences discussed in this case except for that of Egypt (CR = 62.5%) (Botros *et al.,* 2005). On the other hand the results from Kibwezi, an endemic area in Kenya (67.1%) are comparable to findings in this study at one year post-treatment (Thiong'o *et al.*, 2002).

Infection status of *S. mansoni* in this study is highly comparable to that recorded in Ethiopia, with majority of infection at baseline and one year after treatment being low despite the intensity being majorly moderate eight weeks after treatment (Bajiro *et al.,* 2016). In contrast, the infection status of *S. haematobium* was majorly light in all the three periods: from baseline to eight weeks and one year after treatment. These two infection intensities similarly indicated a low intensity that is very much comparable to reports from Timuga and Waja (Dejenie *et al.,* 2010) and Mekelle city (Assefa *et al.,* 2013). In contrast to this, moderate infection intensities have been reported from Wollega (Haile *et al.,* 2012) and Sanje Town (Worku *et al.,* 2014) in Ethiopia and in Yemen (Abdulrab *et al.,* 2013). The difference could be explained through either of the following as previously described: the frequency of students' contact with contaminated water-bodies and the burden of the adult worms hosted (Bajiro *et al.,* 2016)

High prevalences of *S. masoni* and *S. haematobium* have been reported in the past in this study area (Katamine *et al.,* 1978). It is obvious that community members in this endemic area are in constant continuous contact with infested waters from rivers and canals, as there are no other sources of water (Refer to Figure 11). These water sources are responsible for the continuous cycle of infection and reinfection. The community members may not be aware that they are at risk when they come into contact with the water, as there is high dependence on this water for irrigation and daily domestic activities. In view of this treatment should be combined with other measures such as health education access to safe water and snail control, so as to reduce the prevalence to manageable levels in an effort to eliminate infections.

4.3 A. The IgE profile in the primary school children infected with schistosomiasis at baseline and after treatment with praziquantel

Adult worms, inhabiting human host's 'seems' to be impervious to immune attack. Various means are likely to be accountable for the long-term survival of worm in what is perceived to be a hostile immune surrounding. Some of the means of survival may be attributed to the ability of schistosomes to continually renew its outer tegument through unique somatic stem cells (Collins *et al.,* 2013) or by acquiring host antigens (Goldring *et al.,* 1976; Keating *et al.,* 2006). Other facets of their survival may also involve manipulation of and by the host's immune responses, such as isotypic shifts in antibody specificities (Walter *et al.,* 2006; Jiz *et al.,* 2009) and immunoregulation. Although schistosome worms inhabit the human body without immediate grave morbidity, an immune response is always mounted, as the host immune system recognizes the schistosome worm and eggs as foreign.

In this current study, the primary school children displayed high IgE levels before treatment as compared to the period after treatment. Treatment with Praziquantel plays an important role in establishing and maintaining immune response during and after infection. Successful treatment of schistosomiasis with Praziquantel depends on having established immune mechanisms that can kill the worms if they have undergone sufficient surface damage after the paralysis caused by the drug (Fallon *et al.,* 1992; Doenhoff *et al.,* 2008; Brindley *et al.,* 1987)

It was worth noting that there was an inverse relationship between SEA and SWAP antigens in this study. This study further revealed that there was no association between IgE and the intensity of infection. IgE immune responses against SEA were observed to be high in the period before treatment and showed a decrease after treatment, whereas responses for soluble worm antigen

were seen to invariably increase in the period after treatment. In spite of the community in which schistosome immune studies are conducted, there is a prevailing degree of difference in the pattern of immune responses against soluble worm antigens compared to soluble egg antigens (Williams *et al.,* 1994). In a majority of studies, this is observed as high-level responses of individuals with premature infections to soluble egg antigens that then decrease as infections become chronic (Colley *et al.,* 1977; Barsoum *et al.,* 1982; Colley *et al.,* 1986; Grogan *et al.,* 1998; Joseph *et al.,* 2004; Caldas *et al.,* 2008). Responses to soluble worm antigenic preparations (SWAP), in contrast, remain consistently high during early infection and continue to be expressed all through the chronic infections. It is also important to distinguish the history of people being studied beyond current infection with schistosomiasis by taking into consideration how long they have been infected (Black *et al.,* 2010), whether the mothers of current children under study were infected during pregnancy (Eloi-Santos *et al.,* 1989; Novato-Silva *et., al* 1992). Another important factor to consider is whether the study subject had been previously treated with praziquantel and how often (Karanja *et al.,* 2002; Mwinzi *et al.,* 2009;Wanatabe *et al* 2007; Black *et al* 2010) . There is a possibility that these factors could contribute to the current immune status of the child.

In this current study, re infection after treatment was also observed in *S. haematobium* infection. A higher IgE level was recorded in four children that tested positive for *S. haematobium* before and eight weeks after treatment with Praziquantel. The IgE OD level was 0.1766 before treatment and 0.072 after treatment. Interestingly none of the children who had dual infection before treatment tested positive for either *S. mansoni* or *S. haematobium* after treatment. This signifies that Praziquantel is efficient in clearing dual infection in an individual. It also eliminates the double burden of disease in the children who had tested positive for dual infection. The IgE profile showed a remarkable decrease, the mean IgE OD levels decreased significantly (p-value<0.0001) from 0.118 to 0.068. This change in IgE levels indicates that the antigen levels were significantly reduced.

Other studies have shown that following treatment of adults, the adult worm-specific IgE levels either increases or is maintained at pretreatment levels. In children, who are more likely to become reinfected, treatment is less likely to increase the level of IgE/IgG4 ratio, an indication that IgE levels would be maintained or remain reduce (Walter *et al.,* 2006 and Webster *et al.,* 1996). Recent studies have shown that, certain *S. mansoni* adult worm-associated tegumental-allergen-like (TAL) proteins have been identified as important potential targets of protective IgE and reinfection-associated IgG4 (de Moira *et al.,* 2010).

4.3 B. Relationship between IgE antibody levels with age among primary school children infected with schistosomiasis.

Typical age-infection curves normally observed in communities' endemic with schistosomiasis, show infection intensities to be high in early adolescence and to decline as age increases. This pattern is thought to be due to acquired immunity to infection. In support of this, IgE antibody levels to worm antigens, which have been linked to resistance to reinfection (Caldas *et al.,* 2000; Dunne *et al.,* 1992; Hagan *et al.,* 1991; Satti *et al.,* 1996; Webster *et al.,* 1996) tend to increase with age, whereas antibody levels to egg antigens generally decline or are unchanged (Webster *et al.,* 1997; Naus *et al.,* 2003)

In this current study, it was observed that there was an increase in IgE OD levels with age. The IgE OD levels in response to SEA increased from 0.124 at age group 5-7 to 0.134 at age group 8-10. A similar situation was also observed after treatment with Praziquantel, where the IgE OD levels increased from 0.063 units at age group 5-7 to 0.07 units at age group 8-10.

Other similar studies have showed that, Praziquantel treatment boosts the anti-worm IgE immune responses associated with protection in older individuals (Black *et al.,* 2010). This suggests that the 3-5 years age groups may equally gain immunologically from praziquantel, which reduces reinfection in older children and adults by stimulating IgE responses (F Mutapi *et al.,* 2003, Black *et al.,* 2010).

For both *Schistosoma mansoni* and *S. haematobium* responses directed against egg antigen, levels of IgE have been shown to increase with age (Demeure *et al.,* 1993, Butterworth *et al.,* 1988, Hagan *et al.,* 1991, Dunne *et al.,* 1992a,b, Grogan *et al.,* 1998, Ndhlovu *et al.,* 1996, Vandam *et al.,* 1996, Mutapi *et al.,* 1997, Webster *et al.,* 1997). The explanations for these patterns have been controversial. They include the development of acquired resistance which is related to the development of parasite-specific immune responses as a function of the duration and frequency of exposure to parasite antigens. Immune responses are believed to develop slowly and to be short lived (Woolhouse & Hagan 1999), so that as the hosts age, their cumulative experience of parasite antigens increases, resulting in an increase in acquired resistance. This explanation is supported by both experimental (Crombie & Anderson 1985) and field studies (Woolhouse *et al.,* 1991, Woolhouse 1998).

The study showed that treatment altered the relationship between the level of antibody produced and age for the isotypes IgE, IgM, IgG1 and IgG2. In all isotypes pretreatment antibody levels increased with age. This is partly expected in this age-group where exposure to infective water also increases with age, so that the increase in antibody levels is attributed partly to increased exposure to parasite antigens (Woolhouse *et al.,* 1991).

In this current study The IgE OD level increased by 0.000875 against SEA for every additional increase in the age of the children after treatment. Likewise for SWAP antigen, there was an

increase in IgE OD level by 0.001 for every one year increase in the children with age after treatment with Praziquantel.

More recent studies have shown that treatment with Praziquantel has enhanced immune response quantitatively and qualitatively**.** A study conducted in an endemic area in Mashonaland East Province of Zimbabwe, showed that six weeks after treatment all of the treated children were schistosome egg negative. It was further observed that adult worm and egg-specific IgE titers increased significantly following treatment (Rujeni *et al.,* 2013).

4.4 Conclusions and Recommendations

4.4.1 Conclusions

The findings of this study clearly indicate that the prevalence of infection in Taveta Sub County is worth noting. Even after the annual Kenya National government deworming program for primary school children, there are still significant levels of infection. In addition some of the pupils have dual infections with both *S. mansoni* and *S. haematobium,* indicating double morbidity.

Treatment with praziquantel plays a significant role in reducing the prevalence of infection with schistosomiasis, resulting in a decrease in the risk of infection.

STH are not prevalent in the study area. The very low prevalences (>1%), indicate that either the mass deworming programme in the primary school children is successful and that there is ample sanitation among the school children.

There were high IgE levels before treatment as compared to eight weeks after treatment. Praziquantel plays an important role by unmasking the tegument of the schistosome worm therefore increasing the antibody antigen reaction. Praziquantel therefore boosts the IgE immune response following treatment.

There was an increase in IgE levels with age.

4.4.2 Recommendations

1. An overhaul of public health curative measures. The area is endemic for dual schistosomiasis infection therefore more stringent preventive measures need to be put in place so that uninfected children are protected, while those already infected get continuous treatment**.**
2. The results of this study suggest that it is necessary not only for continued preventive and curative chemotherapy intervention for schistosomiasis in the primary school children, but also in the larger adult community
3. Longitudinal studies need to be done, to study the immunity of children infected with schistosomiasis so that more conclusive findings can be made.
4. Treatment with Praziquantel should be repeated after at least 6 months, so as to reduce the reinfection rates and also the risk of infection
5. Monitoring of infection and treatment with albendazole when necessary should be continued as infections with STH were remarkably low.

REFERENCES

Abdulrab, A.; Salem, A.; Algobati, F.; Saleh, S.; Shibani, K. and Albuthigi, R. (2013) Effect of school based treatment on the prevalence of schistosomiasis in endemic area in Yemen. *Iranian Journal of Parasitology*, 8(2) 219–226.

Ahmed, A.M.; Abbas, H.; Mansour, F.A.; Gasim, G.I. and Adam, I. (2012) Schistosoma haematobium infections among schoolchildren in central Sudan one year after treatment with praziquantel. *Parasites & Vectors*, 5(1) 108.

Alberts, B.; Johnson, A.; Lewis, J.; Raff, M.; Roberts, K. and Walter, P. (2002) DOI: 10.1091/mbc.E14-10-1437. *Molecular Biology of the Cell*.

Alemu, A.; Atnafu, A.; Addis, Z.; Shiferaw, Y.; Teklu, T.; Mathewos, B.; Birhan, W.; Gebretsadik, S. and Gelaw, B. (2011) Soil transmitted helminths and schistosoma mansoni infections among school children in Zarima town, northwest Ethiopia. *BMC infectious diseases*, 11(1) 189–189.

Andrade, A. and Cheever, A.W. (1971) Alterations of the intrahepatic vasculature in hepatosplenic schistosomiasis mansoni. Am J Trop Med Hyg.

Anto, F.; Asoala, V.; Adjuik, M.; Anyorigiya, T.; Oduro, A.; Akazili, J.; Akweongo, P.; Ayivor, P. and Hodgson, L.B. and A. (2013) Water Contact Activities and Prevalence of Schistosomiasis Infection among School-age Children in Communities along an Irrigation Scheme in Rural Northern Ghana. *Journal of Bacteriology & Parasitology*, 04(04).

Assefa, a; Dejenie, T. and Tomass, Z. (2013) Infection prevalence of Schistosoma mansoni and associated risk factors among schoolchildren in suburbs of Mekelle city, Tigray, Northern Ethiopia. *Momona Ethiopian Journal of Science*, 5(1) 174–188.

Awasthi, S.; Pande, V.K. and Fletcher, R.H. (2000) Effectiveness and cost-effectiveness of albendazole in improving nutritional status of pre-school children in urban slums. *Indian pediatrics*, 37(1) 19–29.

Bajiro, M.; Dana, D.; Ayana, M.; Emana, D.; Mekonnen, Z.; Zawdie, B.; Garbi, A.; Kure, A.; Zeynudin, A.; Cheesbrough, M.; Engels, D.; Chitsulo, L.; Montresor, A.; Savioli, L.; Steinmann, P.; Keiser, J.; Bos, R.; Tanner, M.; Utizinger, J.; Lo, C.; Kloos, H.; Birrie, H.;

Cioli, D.; Pica-Mattoccia, L.; Archer, S.; Utzinger, J.; Keiser, J.; Sabah, A.; Fletcher, C.; Webbe, G.; Doenhoff, M.; Utzinger, J.; N'Goran, E.; N'dri, A.; Lengeler, C.; Tanner, M.; Gryseels, B.; Polderman, A.; Engels, D.; Tweyongyere, R.; Mawa, P.; Kihembo, M.; Jones, F.; Webb, E.; Coses, S.; Botros, S.; Sayed, H.; Amer, N.; El-Ghannam, M.; Bennett, J.; Day, T.; Melman, S.; Steinauer, M.; Cunningham, C.; Kubatko, L.; Mwangi, I.; Wynn, N.; Tchuente, L.T.; Momo, S.; Stothard, J.; Rollinson, D.; Anto, F.; Asoala, V.; Adjuik, M.; Anyorigiya, T.; Oduro, A.; Akazili, J.; Banji, B.; Babadoko, M.; Mohammed, G.; Barbosa, C.; Favre, T.; Wanderley, T.; Callou, A.; Pieri, O.; Goselle, N.; Anegbe, D.; Imandeh, G.; Dakul, D.; Onwuliri, A.; Abba, O.; Tadesse, D.; Tsehaye, A.; Yami, A.; Mamo, Y.; Kebede, S.; Mazigo, D.; Waihenya, R.; Mkoji, M.; Zinga, M.; Ambrose, E.; Jahanpour, F.; Abebe, N.; Erko, B.; Medhin, G.; Nega, B.; Haile, S.; Golassa, L.; Mekonnen, Z.; John, R.; Ezekiel, M.; Philbert, C.; Andrew, A.; Assefa, A.; Dejenie, T.; Tomass, Z.; Legesse, M.; Erko, B.; Dejenie, T.; Asmelash, T.; Abdelkadir, M.; Picquet, M.; Vercruysse, J.; Shaw, D.; Diop, M.; Ly, A.; Nega, B.; Gunar, G.S.; Fekadu, A.; Hailu, B.; Girmay, M.; Teferi, G.; Danso-Appiah, A.; Vlas, S.; Garba, A.; Lamine, M.; Barkiré, N.; Djibon, A.; Sofo, B.; Gouvras, A.; Hagan, P.; Coles, G.; Kusel, J.; Tchuem-Tchuente, L.; Amin, M.; Swar, M.; Kardaman; Elhussein, D.; Nouman, G.; Mahmound, A.; Kihara, J.; Muhoho, N.; Njomo, D.; Mwobobia, I.; Josyline, K.; Mitsui, Y.; Degu, G.; Mengistu, G. and Jones, J. (2016) Prevalence of Schistosoma mansoni infection and the therapeutic efficacy of praziquantel among school children in Manna District, Jimma Zone, southwest Ethiopia. *Parasites & Vectors*, 9(1) 560–560.

Banji, B.; Babadoko, M. and Mohammed, G. (2012) Survey Of Schistosomiasis And Other Intestinal Helminthiases Among School-Aged Children in Agaie, Niger State Nigeria. *Journal of Pharmaceutical and Biomedical Sciences*, 15(07) 1–5.

Barakat, R.M.R. (2013) Epidemiology of Schistosomiasis in Egypt. Travel through time review.

Barsoum, I.S.; Gamil, F.M.; Al-Khafif, M.A.; Ramzy, R.M.; El Alamy, M.A. and Colley, D.G. (1982) Immune responses and immunoregulation in relation to human schistosomiasis in Egypt. I. Effect of treatment on in vitro cellular responsiveness. *Am J Trop Med Hyg*, 31(6) 1181–1187.

Black, C.L.; Muok, E.M.O.; Mwinzi, P.N.M.; Carter, J.M.; Karanja, D.M.S.; Secor, W.E. and Colley, D.G. (2010) Increases in levels of schistosome-specific immunoglobulin E and CD23(+) B cells in a cohort of Kenyan children undergoing repeated treatment and

reinfection with Schistosoma mansoni. *The Journal of infectious diseases*, 202(August) 399–405.

Black, C.L.; Mwinzi, P.N.M.; Muok, E.M.O.; Abudho, B.; Fitzsimmons, C.M.; Dunne, D.W.; Karanja, D.M.S.; Secor, W.E. and Colley, D.G. (2010) Influence of exposure history on the immunology and development of resistance to human Schistosomiasis mansoni. *PLoS neglected tropical diseases*, 4(3) e637–e637.

Bleakley, H. (2003) Disease and Development: Evidence from the American South. *Journal of the European Economic Association*, 1(2-3) 376–386.

Booth, M; Shaw, M.A. and Carpenter, D.(2006). Carriage of DRB1*13 is associated with increased posttreatment IgE levels against *Schistosoma mansoni* antigens and lower long-term reinfection levels. J Immunol.

Botros, S.; Sayed, H.; El-Dusoki, H.; Sabry, H.; Rabie, I.; El-Ghannam, M.; Hassanein, M.; El-Wahab, Y.A. and Engels, D. (2005) Efficacy of mirazid in comparison with praziquantel in Egyptian Schistosoma mansoni-infected school children and households. *American Journal of Tropical Medicine and Hygiene*, 72(2) 119–123.

Brindley, P.J. and Sher, A. (1987) The chemotherapeutic effect of praziquantel against Schistosoma mansoni is dependent on host antibody response. *The Journal of Immunology*, 139(1) 215–220.

Brooker, S. (2010) DOI: 10.1016/j.ijpara.2010.04.004 PMID: 20430032. *Estimating the global distribution and disease burden of intestinal nematode infections: Adding up the numbers - A review*. 10. Vol. 40.

Brooker, S.; Kabatereine, N.B.; Fleming, F. and Devlin, N. (2008) Cost and cost-effectiveness of nationwide school-based helminth control in Uganda: Intra-country variation and effects of scaling-up. *Health Policy and Planning*, 23(1) 24–35.

Bustinduy, A.L. and Thomas, C.L, Fiutem J.J. (2011). Measuring fitness of Kenyan children with polyparasitic infections using the 20-meter shuttle run test as morbidity metric. PLoS Negl Trop Dis.

Butterworth, A.; Dunne, D.; Anthony, F.; Capron, M.; Khalife, J.; Capron, A.; Koech, D.; Ouma, J. and Sturrock, R. (1988) Immunity in human schistosomiasis mansoni: Cross-reactive IgM and IgG2 anti-carbohydrate antibodies block the expression of immunity. *Biochimie*, 70(8) 1053–1063.

Butterworth, A.E.; Curry, A.J.; Dunne, D.W.; Fulford, A.J.; Kimani, G.; Kariuki, H.C.; Klumpp, R.; Koech, D.; Mbugua, G. and Ouma, J.H. (1994) Immunity and morbidity in human schistosomiasis mansoni. *Tropical and geographical medicine*, 46(4 Spec No) 197–208.

Butler, S.E; Muok, E.M. and Montgomery, S.P. (2012). Mechanism of anemia in *Schistosoma mansoni*-infected school children in Western Kenya. Am J Trop Med Hyg.

Caldas, I.R.; Campi-Azevedo, A.C.; Oliveira, L.F.A.; Silveira, A.M.S.; Oliveira, R.C. and Gazzinelli, G. (2008) Human schistosomiasis mansoni: Immune responses during acute and chronic phases of the infection. *Acta Tropica*, 108(2-3) 109–117.

Caldas, I.R; Correa-Oliveira R; Colosimo, E; Carvalho, O.S and Massara C.L. (2000) Susceptibility and resistance to *Schistosoma mansoni* reinfection: parallel cellular and isotypic immunologic assessment. Am J Trop Med Hyg

CDC - Schistosomiasis (2014) Available from https://www.cdc.gov/parasites/schistosomiasis

Chitsulo, L.; Engels, D.; Montresor, A. and Savioli, L. (2000) The global status of schistosomiasis and its control. *Acta Tropica*, 77(1) 41–51.

Colley, D.G.; Cook, J.A.; Freeman, G.L.; Bartholomew, R.K. and Jordan, P. (1977) Immune responses during human schistosomiasis mansoni: in vitro lymphocyte blastogenic responses to heterogeneous antigenic preparations from schistosome, worms and cercariae. *International Archives of Allergy and Immunology*, 53(5) 420–433.

Colley, D.G.; Garcia, A.A.; Lambertucci, J.R.; Parra, J.C.; Katz, N.; Rocha, R.S. and Gazzinelli, G. (1986) Immune responses during human schistosomiasis: XII. Differential responsiveness in patients with hepatosplenic disease. *American Journal of Tropical Medicine and Hygiene*, 35(4) 793–802.

Colley, D.G.; Montesano, M.;, Freeman, G.L. and Secor W,E.(1999) Infection-stimulated or perinatally initiated idiotypic interactions can direct differential morbidity and mortality in schistosomiasis. Microbes Infect.

Collins 3rd, J.J.; Wang, B.; Lambrus, B.G.; Tharp, M.E.; Iyer, H. and Newmark, P.A. (2013) Adult somatic stem cells in the human parasite *Schistosoma mansoni*. *Nature*, 494(7438) 476–479.

Crombie, J.A. and Anderson, R.M. (1985) Population dynamics of *Schistosoma mansoni* in mice repeatedly exposed to infection. *Nature*, 315(6019) 491–493.

van Dam, G.J.; Stelma, F.F.; Gryseels, B.; Falcão Ferreira, S.T.; Talla, I.; Niang, M.; Rotmans, J.P. and Deelder, A. M. (1996) Antibody response patterns against *Schistosoma mansoni* in a recently exposed community in Senegal. *The Journal of infectious diseases*, 173(5) 1232–41.

Da Silva, I.M.; Thiengo, R.; Conceição, M.J.; Rey, L.; Lenzi, H.L.; Filho, E.P. and Ribeiro, P.C. (2005) Therapeutic failure of praziquantel in the treatment of *Schistosoma haematobium* infection in Brazilians returning from Africa. *Memorias do Instituto Oswaldo Cruz*, 100(4) 445–449.

Davis, S.M.; Worrell, C.M.; Wiegand, R.E.; Odero, K.O.; Suchdev, P.S.; Ruth, L.J.; Lopez, G.; Cosmas, L.; Neatherlin, J.; Njenga, S.M.; Montgomery, J.M. and Fox, L.M. (2014) Soil-transmitted helminths in pre-school-aged and school-aged children in an urban slum: A cross-sectional study of prevalence, distribution, and associated exposures. *American Journal of Tropical Medicine and Hygiene*, 91(5) 1002–1010.

Debalke, S.; Worku, A.; Jahur, N. and Mekonnen, Z. (2013) Soil transmitted helminths and associated factors among schoolchildren in government and private primary school in Jimma Town, Southwest Ethiopia. *Ethiopian journal of health sciences*, 23(3) 237–44.

Dejenie, T. and Asmelash, T. (2010) Schistosomiasis mansoni among school children of different water source users in Tigray, northern Ethiopia. *Momona Ethiopian Journal of Science*, 2(1).

Dejenie, T.; Asmelash, T. and Abdelkadir, M. (2010) Efficacy of Praziquantel in Treating Schistosoma Mansoni Infected School Children in Tumuga and Waja, North Ethiopia. *Mejs*, 2(2) 3–11.

Dessein, A.J.; Demeure, C.E.; Rihet, P.; Abel, L.; Ouattara, M. and Bourgois, A. (1993) Resistance to Schistosoma mansoni in Humans: Influence of the IgE/IgG4 Balance and IgG2 in Immunity to Reinfection after Chemotherapy. *Journal of Infectious Diseases*, 168(4) 1000–1008.

Doenhoff, M.J.; Cioli, D. and Utzinger, J. (2008) Praziquantel: mechanisms of action, resistance and new derivatives for schistosomiasis. *Current Opinion in Infectious Diseases*, 21(6) 659–667.

Downs, J.A; Mguta, C and Kaatano, G.M.(2011). Urogenital schistosomiasis in women of reproductive age in Tanzania's Lake Victoria region. Am J Trop Med Hyg.

Dunne, D.W.; Butterworth, A.E.; Fulford, A.J.C.; Curtis Kariuki, H.; Langley, J.G.; Ouma, J.H.; Capron, A.; Pierce, R.J. and Sturrock, R.F. (1992a) Immunity after treatment of human schistosomiasis: association between IgE antibodies to adult worm antigens and resistance to reinfection. *European Journal of Immunology*, 22(6) 1483–1494.

Dunne, D.W; Butterworth, A.E; Fulford, A.J; Ouma, J.H. and , Sturrock, R.F.(1992b) Human IgE responses to *Schistosoma mansoni* and resistance to reinfection. Mem Inst Oswaldo Cruz

Demeure, C.E; Rihet, P; Abel; Ouattara, M; Bourgois, A. and Dessein; A.J. (1993). Resistance to *Schistosoma mansoni* in humans: influence of the IgE/IgG4 balance and IgG2 in immunity to reinfection after chemotherapy. J Infect Dis. 1993

Dunne, D.W.; Butterworth, A.E.; Fulford, A.J.; Ouma, J.H. and Sturrock, R.F. (1992) Human IgE responses to Schistosoma mansoni and resistance to reinfection. *Memorias do Instituto Oswaldo Cruz*, 87 Suppl 4 99–103.

Eloi-Santos, S.M.; Novato-Silva, E.; Maselli, V.M.; Gazzinelli, G.; Colley, D.G. and Correa-Oliveira, R. (1989) Idiotypic sensitization in utero of children born to mothers with schistosomiasis or Chagas' disease. *Journal of Clinical Investigation*, 84(3) 1028–1031.

Ellis MK, Li Y, Hou X, Chen H. McManus DP. (2008) sTNFR-II and sICAM-1 are associated with acute disease and hepatic inflammation in schistosomiasis japonica. Int J Parasitol.

Enk, M.J.; Lima, A.C.L.; Massara, C.L.; Coelho, P.M.Z. and Schall, V.T. (2008) A combined strategy to improve the control of Schistosoma mansoni in areas of low prevalence in Brazil. *American Journal of Tropical Medicine and Hygiene*, 78(1) 140–146.

Erb, K.J. (2007) DOI: 10.1002/eji.200737314 PMID: 17429848. *Helminths, allergic disorders and IgE-mediated immune responses: Where do we stand?* 5. Vol. 37.

Erko, B.; Degarege, A.; Tadesse, K.; Mathiwos, A. and Legesse, M. (2012) Efficacy and side effects of praziquantel in the treatment of Schistosomiasis mansoni in schoolchildren in Shesha Kekele Elementary School, Wondo Genet, Southern Ethiopia. *Asian Pacific Journal of Tropical Biomedicine*, 2(3) 235–239.

Fallon, P.G.; Cooper, R.O.; Probert, A.J. and Doenhoff, M.J. (1992) Immune-dependent chemotherapy of schistosomiasis. *Parasitology*, 105 Suppl S41–8.

Favre, T.C.; Pereira, A.P.B.; Galvão, A.F.; Zani, L.C.; Barbosa, C.S. and Pieri, O.S. (2009) A rationale for schistosomiasis control in Elementary Schools of the Rainforest Zone of Pernambuco, Brazil. *PLoS Neglected Tropical Diseases*, 3(3).

Figueiredo, J.P; Oliveira, R; Cardoso, L,S; Barnes, K.C. and Grant AV (2012) Adult worm-specific IgE/IgG4 balance is associated with low infection levels of *Schistosoma mansoni* in an endemic area. Parasite Immunol

Fitzsimmons, C.M; Jones, F.M; AND Pinot de Moira A. (2012) Progressive cross-reactivity in IgE responses: an explanation for the slow development of human immunity to schistosomiasis? Infect Immun.

Fitzsimmons, C.M; Joseph, S. and Jones FM. (2004). Chemotherapy for schistosomiasis in Ugandan fishermen: treatment can cause a rapid increase in interleukin-5 levels in plasma but decreased levels of eosinophilia and worm-specific immunoglobulin E. Infect Immun. 2004

Fitzsimmons, C.M.; McBeath, R.; Joseph, S.; Jones, F.M.; Walter, K.; Hoffmann, K.F.; Kariuki, H.C.; Mwatha, J.K.; Kimani, G.; Kabatereine, N.B.; Vennervald, B.J.; Ouma, J.H. and Dunne, D.W. (2006) Factors affecting human IgE and IgG responses to allergen-like Schistosoma mansoni antigens: Molecular structure and patterns of in vivo exposure. *International Archives of Allergy and Immunology*, 142(1) 40–50.

Galeta,S; Alemu,A; Getie, S; Mekonnen Z and Berhano E. (2015). Prealence of urinary schistosomiasis and associated risk factors among Abobo primary school children in Gambella. A cross sectional study. Bio Med Central

Garcia, L.S. (2007) Diagnostic Medical Parasitology, Fith Edition. *ASM Press. Washington, DC*, 130–140.

Ganley-Leal, L.M; Mwinzi, P.N.M and Cetre-Sossah C.B(2006). Higher percentages of circulating mast cell precursors correlate with susceptibility to reinfection with *Schistosoma mansoni*. Am J Trop Med Hyg.

Goldring, O.L.; Clegg, J. a; Smithers, S.R. and Terry, R.J. (1976) Acquisition of human blood group antigens by Schistosoma mansoni. *Clinical and experimental immunology*, 26(1) 181–7.

Goselle, N.O.; Anegbe, D.; Imandeh, G.N.; Dakul, D.A.; Onwuliri, A.C.F.; Abba, O.J.; Udeh, O.E. and Abelau, A.M. (2010) Schistosoma mansoni infections amongst school children in Jos, Nigeria. *Science World Journal*, 5(1) 42–45.

Gouvras, A.N.; Kariuki, C.; Koukounari, A.; Norton, A.J.; Lange, C.N.; Ireri, E.; Fenwick, A.; Mkoji, G.M. and Webster, J.P. (2013) The impact of single versus mixed Schistosoma haematobium and *S. mansoni* infections on morbidity profiles amongst school-children in Taveta, Kenya. *CONTRAST alliance: optimized surveillance and sustainable control of schistosomiasis*, 128(2) 309–317.

Greenland, K.; Dixon, R.; Khan, S.A.; Gunawardena, K.; Kihara, J.H.; Smith, J.L.; Drake, L.; Makkar, P.; Raman, S.; Singh, S. and Kumar, S. (2015) The Epidemiology of Soil-Transmitted Helminths in Bihar State, India. *PLoS Neglected Tropical Diseases*, 9(5).

Grogan, J.L.; Kremsner, P.G.; Deelder, a M. and Yazdanbakhsh, M. (1998) Antigen-specific proliferation and interferon-gamma and interleukin-5 production are down-regulated during Schistosoma haematobium infection. *The Journal of infectious diseases*, 177(5) 1433–7.

Grogan, J.L; Kremsner, P.G; Deelder, A.M. and Yazdanbakhsh, M. (1996) Elevated proliferation and interleukin-4 release from CD4+ cells after chemotherapy in human *Schistosoma haematobium* infection. Eur J Immunol.

Gounni, A.S; Lamkhioued, B and Ochiai K. (1994). High-affinity IgE receptor on eosinophils is involved in defence against parasites.

Guidi, A.; Andolina, C.; Makame Ame, S.; Albonico, M.; Cioli, D. and Juma Haji, H. (2010) Praziquantel efficacy and long-term appraisal of schistosomiasis control in Pemba Island. *Tropical Medicine and International Health*, 15(5) 614–618.

Guisse, F.; Polman, K.; Stelma, F.F.; Mbaye, A.; Talla, I.; Niang, M.; Deelder, A.M.; Ndir, O. and Gryseels, B. (1997) Therapeutic evaluation of two different dose regimens of praziquantel in a recent Schistosoma mansoni focus in northern Senegal. *American Journal of Tropical Medicine and Hygiene*, 56(5) 511–514.

Hagan, P.; Blumenthal, U.J.; Dunn, D.; Simpson, A.J.G. and Wilkins, H.A. (1991) Human IgE, IgG4 and resistance to reinfection with Schistosomahaematobium. *Nature*, 349(6306) 243–245.

Haile, S.; Golassa, L. and Mekonnen, Z. (2012) Prevalence of Schistosoma mansoni and effectiveness of Praziquantel in school children in Finchaa valley , Ethiopia. *Journal of Parasitology and Vector Biology*, 4(3) 25–30.

Hokke, C.H; Fitzpatrick, J. M; Hoffman, K.F. (2007) Integrating transcriptome, proteome and glycome analyses of Schistosoma biology. Trends Parasitol.

Janeway, C.A.; Travers, P.; Walport, M. and Shlomchik, M. (2001) DOI: 10.1111/j.1467-2494.1995.tb00120.x PMID: 19245486. *Immunobiology: The Immune System In Health And Disease*.

Joseph, S; Jones, F.M and Laidlaw and M. E.(2004). Impairment of the *Schistosoma mansoni*-specific immune responses elicited by treatment with praziquantel in Ugandans with HIV-1 coinfection. J Infect Dis

Joseph, S; Jones, F.M and Walter, K (2004) Increases in human T helper 2 cytokine responses to *Schistosoma mansoni* worm and worm-tegument antigens are induced by treatment with praziquantel. J Infect Dis.

Jiz, M.; Friedman, J.F.; Leenstra, T.; Jarilla, B.; Pablo, A.; Langdon, G.; Pond-Tor, S.; Wu, H.W.; Manalo, D.; Olveda, R.; Acosta, L. and Kurtis, J.D. (2009) Immunoglobulin E (IgE) responses to paramyosin predict resistance to reinfection with Schistosoma japonicum and are attenuated by IgG4. *Infection and Immunity*, 77(5) 2051–2058.

John, R.; Ezekiel, M.; Philbert, C. and Andrew, A. (2008) Schistosomiasis transmission at high altitude crater lakes in western Uganda. *BMC infectious diseases*, 8(1) 110–110.

Joseph, S.; Jones, F.M.; Kimani, G.; Mwatha, J.K.; Kamau, T.; Kazibwe, F.; Kemijumbi, J.; Kabatereine, N.B.; Booth, M.; Kariuki, H.C.; Ouma, J.H.; Vennervald, B.J. and Dunne, D.W. (2004) Cytokine Production in Whole Blood Cultures from a Fishing Community in an Area of High Endemicity for Schistosoma mansoni in Uganda: The Differential Effect of Parasite Worm and Egg Antigens. *Infection and Immunity*, 72(2) 728–734.

Kabatereine, N.B.; Kemijumbi, J.; Ouma, J.H.; Sturrock, R.F.; Butterworth, A.E.; Madsen, H.; Ørnbjerg, N.; Dunne, D.W. and Vennnervald, B.J. (2003) Efficacy and side effects of praziquantel treatment in a highly endemic Schistosoma mansoni focus at Lake Albert, Uganda. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 97(5) 599–603.

Kamel IA, Elwi AM, Cheever AW, Mosimann JE. (1978) Danner R. *Schistosoma mansoni* and *S. haematobium* infections in Egypt. IV. Hepatic lesions. Am J Trop Med Hyg.

Karanja, D.M.; Hightower, A.W.; Colley, D.G.; Mwinzi, P.N.; Galil, K.; Andove, J. and Secor, W.E. (2002) Resistance to reinfection with Schistosoma mansoni in occupationally exposed adults and effect of HIV-1 co-infection on susceptibility to schistosomiasis: a longitudinal study. *The Lancet*, 360(9333) 592–596.

Katamine, D.; Siongok, T.A.; Kawashima, K.; Nakajima, Y.; Nojima, H. and Imai, J. (1978) Prevalence of Human Schistosomiasis in The Taveta Area of Kenya, East Africa. *Japanese Journal of Tropical Medicine and Hygiene*, 6(3-4) 167–180.

Keating, J.H.; Wilson, R.A. and Skelly, P.J. (2006) No overt cellular inflammation around intravascular schistosomes in vivo. *The Journal of parasitology*, 92(6) 1365–9.

Keiser, J.; Chollet, J.; Xiao, S.H.; Mei, J.Y.; Jiao, P.Y.; Utzinger, J. and Tanner, M. (2009) Mefloquine - An aminoalcohol with promising antischistosomal properties in mice. *PLoS Neglected Tropical Diseases*, 3(1).

King, C.H.; Muchiri, E.M. and Ouma, J.H. (2000) Evidence against rapid emergence of praziquantel resistance in Schistosoma haematobium, Kenya. *Emerging Infectious Diseases*, 6(6) 585–594.

King CH, Dickman K. Tisch DJ. (2005) Reassessment of the cost of chronic helmintic infection: a meta-analysis of disability-related outcomes in endemic schistosomiasis. Lancet.

Kjetland EF, Ndhlovu PD, Gomo E, (2006). Association between genital schistosomiasis and HIV in rural Zimbabwean women. AIDS.

Leenstra, T; Acosta, L.P and Wu, H.W.(2006) T-helper-2 cytokine responses to Sj97 predict resistance to reinfection with *Schistosoma japonicum*. Infect Immun.

Leenstra T, Acosta LP, Langdon GC, (2006). Schistosomiasis japonica, anemia, and iron status in children, adolescents, and young adults in Leyte, Philippines 1. Am J Clin Nutr.

Lewert, R.M. and Mandlowitz, S. (1969) Schistosomiasis: prenatal induction of tolerance to antigens. Nature.

Li, Y; Sleigh, A.C; Ross, A.G; Zhang, X and Williams, G.M. (2001) Human susceptibility to *Schistosoma japonicum* in China correlates with antibody isotypes to native antigens. Trans R Soc Trop Med Hyg

Liang, Y.S.; Coles, G.C. and Doenhoff, M.J. (2000) Short communication: Detection of praziquantel resistance in schistosomes. *Tropical Medicine and International Health*, 5(1) 72–72.

von Lichtenberg F.(1964) Studies on granuloma formation. III. Antigen sequestration and destruction in the schistosome peudotubercle. Am J Pathol.

Liu, F:, Lu, J:, Hu,W; (2006)New perspectives on host-parasite interplay by comparative transcriptomic and proteomic analyses of *Schistosoma japonicum*. PLoS Pathog.

Maizels, R.M. and Yazdanbakhsh, M. (2003) Immune regulation by helminth parasites: cellular and molecular mechanisms. Nat Rev Immunol.

Malaquias, L.C; Falcão, P. and Silveira, A.M, (1997). Cytokine regulation of human immune response to *Schistosoma mansoni*: analysis of the role of IL-4, IL-5 and IL-10 on peripheral blood mononuclear cell responses. Scand J Immunol.

Mallery, D.L.; McEwan, W.A.; Bidgood, S.R.; Towers, G.J.; Johnson, C.M. and James, L.C. (2010) Antibodies mediate intracellular immunity through tripartite motif-containing 21 (TRIM21). *Proceedings of the National Academy of Sciences*, 107(46) 19985–19990.

Masaku, J.; Madigu, N.; Okoyo, C. and Njenga, S.M. (2015) Current status of Schistosoma mansoni and the factors associated with infection two years following mass drug administration programme among primary school children in Mwea irrigation scheme: A cross-sectional study. *BMC Public Health*, 15(1) 739.

Massara, C.L.; Peixoto, S.V.; Enk, M.J.; da Silva Barros, H.; dos Santos Carvalho, O.; Sakurai, E. and Schall, V. (2006) Evaluation of an improved approach using residences of schistosomiasis-positive school children to identify carriers in an area of low endemicity. *The American journal of tropical medicine and hygiene*, 74(3) 495–499.

Mazigo, H.D.; Nuwaha, F.; Kinung'hi, S.M.; Morona, D.; de Moira, A.P.; Wilson, S.; Heukelbach, J. and Dunne, D.W. (2012) Epidemiology and control of human schistosomiasis in Tanzania. *Parasites & Vectors*, 5(1) 274.

Medhat, A; Shehata and , Bucci, K. (1998). Increased interleukin-4 and interleukin-5 production in response to *Schistosoma haematobium* adult worm antigens correlates with lack of reinfection after treatment. J Infect Dis.

Mendis, S; Funiko, K; Cameron, A; Laing, R; Filipe Jr A; Lewoski, J. (2007). A systematic review of inequalities in the use of maternal health care in developing countries. Bull World Health Organ.

Mitchell, K.M; Mutapi, F;Savill, N.J. and Woolhouse M.E (2011) Explaining observed infection and antibody age-profiles in populations with urogenital schistosomiasis. PLoS Comput Biol.

de Moira, A.P.; Fulford, A.J.C.; Kabatereine, N.B.; Ouma, J.H.; Booth, M. and Dunne, D.W. (2010) Analysis of Complex Patterns of Human Exposure and Immunity to Schistosomiasis mansoni: The Influence of Age, Sex, Ethnicity and IgE. *Plos Neglected Tropical Diseases*, 4(9) e820.

Montreso,r A; Crompton, D.W.T, Gyorkos, T.W; and Saviolli (2002). Helminth control in School age children: a gide for managers of control programmes, WHO, Geneva.

Montresor, A.; Gabrielli, A.F.; Diarra, A. and Engels, D. (2010) Estimation of the cost of large-scale school deworming programmes with benzimidazoles. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 104(2) 129–132.

Mutahi, W.T. and Thiong'O, F.W. (2005) PMID: 16463753. *Prevalence and intensity of Schistosomiasis mansoni in irrigation and non-irrigation areas of Central Kenya*. 11. Vol. 82.

Mutapi, F.; Burchmore, R.; Mduluza, T.; Foucher, A.; Harcus, Y.; Nicoll, G.; Midzi, N.; Turner, C.M. and Maizels, M.R. (2005) Praziquantel Treatment of Individuals Exposed to Schistosoma haematobium Enhances Serological Recognition of Defined Parasite Antigens. *Journal of Infectious Diseases*, 192(6) 1108–1118.

Mutapi, F.; Burchmore, R.; Mduluza, T.; Midzi, N.; Turner, C.M.R. and Maizels, R.M. (2008) Age Related and Infection Intensity–Related Shifts in Antibody Recognition of Defined Protein Antigens in a Schistosome Exposed Population. *The Journal of Infectious Diseases*, 198(2) 167–75.

Mutapi, F.; Hagan, P.; Woolhouse, M.E.J.; Mduluza, T. and Ndhlovu, P.D. (2003) Chemotherapy-induced, age-related changes in antischistosome antibody responses. *Parasite Immunology*, 25(2) 87–97

Mutapi, F. Billingsley, P.F and Secor, W.E (2013). Infection and treatment immunizations for successful parasite vaccines. Trends Parasitol.

Mutapi, F.; Ndhlovu, P.D.; Hagan, P.; Spicer, J.T.; Mduluza, T.; Turner, C.M.; Chandiwana, S.K. and Woolhouse, M.E. (1998a) Chemotherapy accelerates the development of acquired immune responses to Schistosoma haematobium infection. *J Infect Dis*, 178(1) 289–293.

Mutapi, F.; Ndhlovu, P.D.; Hagan, P. and Woolhouse, M.E.J. (1998b) Changes in specific anti-egg antibody levels following treatment with praziquantel for Schistosoma haematobium infection in children. *Parasite Immunology*, 20(12) 595–600.

Mutapi, F.; Rujeni, N.; Bourke, C.; Mitchell, K.; Appleby, L.; Nausch, N.; Midzi, N. and Mduluza, T. (2011) Schistosoma haematobium treatment in 1-5 year old children: Safety and efficacy of the antihelminthic drug praziquantel. *PLoS Neglected Tropical Diseases*, 5(5).

Mutapi, F,; Ndhlovu, P.D; Hagan, P. and Woolhouse, M.E (1999). A comparison of re-infection rates with *Schistosoma haematobium* following chemotherapy in areas with high and low levels of infection. Parasite Immunol.

Mwinzi, P.N.M.; Ganley-Leal, L.; Black, C.L.; Secor, W.E.; Karanja, D.M.S. and Colley, D.G. (2009) Circulating CD23+ B cell subset correlates with the development of resistance to Schistosoma mansoni reinfection in occupationally exposed adults who have undergone multiple treatments. *The Journal of infectious diseases*, 199(2) 272–9.

Nagi, S.; Chadeka, E.A.; Sunahara, T.; Mutungi, F.; Justin, Y.K.; Kaneko, S.; Ichinose, Y.; Matsumoto, S.; Njenga, S.M.; Hashizume, M.; Shimada, M. and Hamano, S. (2014) Risk factors and spatial distribution of Schistosoma mansoni infection among primary school children in Mbita District, Western Kenya. *PLoS Neglected Tropical Diseases*, 8 (7) e2991.

Naus ,C.W; van Dam, G.J; Kremsner, P.G; Krijger, F.W and Deelder AM (1998) Human IgE, IgG subclass, and IgM responses to worm and egg antigens in schistosomiasis haematobium: a 12-month study of reinfection in Cameroonian children. Clin Infect Dis

Naus, C.W.A.; Booth, M.; Jones, F.M.; Kemijumbi, J.; Vennervald, B.J.; Kariuki, C.H.; Ouma, J.H.; Kabatereine, N.B. and Dunne, D.W. (2003) The relationship between age, sex, egg-count and specific antibody responses against Schistosoma mansoni antigens in a Ugandan fishing community. *Tropical Medicine and International Health*, 8(6) 561–568.

Nausch, N; Midzi, N; Mduluza, T; Maizels, R.M. and Mutapi F. (2011) Regulatory and activated T cells in human *Schistosoma haematobium* infections. PLoS ONE.

Ndhlovu, P.; Cadman, H.; Vennervald, B.J.; Christensen, N.O.; Chidimu, M. and Chandiwana, S.K. (1996) Age-related antibody profiles in Schistosoma haematobium infections in a rural community in Zimbabwe. *Parasite Immunology*, 18(4) 181–191.

Njaanake, K.H.; Vennervald, B.J.; Simonsen, P.E.; Madsen, H.; Mukoko, D.A.; Kimani, G.; Jaoko, W.G. and Estambale, B.B. (2015) Schistosoma haematobium and soil-transmitted Helminths in Tana Delta District of Kenya: infection and morbidity patterns in primary schoolchildren from two isolated villages. *BMC Infectious Diseases*, 16(1) 57.

Nordberg, E.; Carter, J.; King, B.; Nduba, J.; Some, E. and Aluvaala, B. (1999) *Communicable diseases: A Manual for Health Workers in Sub-Saharan Africa*. Rural health series 7. 3rd ed. African Medical and Research Foundation (AMREF).

Novato-Silva, E.; Gazzinelli, G. and Colley, D.G. (1992) Immune responses during human schistosomiasis mansoni. XVIII. Immunologic status of pregnant women and their neonates. *Scand J Immunol*, 35(4) 429–437.

Odiere, M.R.; Rawago, F.O.; Ombok, M.; Secor, W.E.; Karanja, D.M.; Mwinzi, P.N.; Lammie, P.J. and Won, K. (2012) High prevalence of schistosomiasis in Mbita and its adjacent islands of Lake Victoria, western Kenya. *Parasites & Vectors*, 5(1) 278.

Odinaka, K.K.; Nwolisa, E.C.; Mbanefo, F.; Iheakaram, A.C. and Okolo, S. (2015) Prevalence and Pattern of Soil-Transmitted Helminthic Infection among Primary School Children in a Rural Community in Imo State, Nigeria. *Journal of Tropical Medicine*,

Owogu, S.E; Ramamurthy, N.K;Kabatereine,N.B.;nKazibwe, F.;Tukahebwa, E.;Webster,J.P.;Fenwic,A. and Stothard, J.R.(2006). Schistosoma mansoni in infants (aged less than 3 years) along the Ugandan shoreline of Lak Victoria. Annals of Trooical Medicine and Parasitology.

Ojurongbe, O.; Sina-Agbaje, O.R.; Busari, A.; Okorie, P.N.; Ojurongbe, T.A. and Akindele, A.A. (2014) Efficacy of praziquantel in the treatment of Schistosoma haematobium infection among school-age children in rural communities of Abeokuta, Nigeria. *Infectious diseases of poverty*, 3(1) 30–30.

Olds, G.R.; King, C.; Hewlett, J.; Olveda, R.; Wu, G.; Ouma, J.; Peters, P.; McGarvey, S.; Odhiambo, O.; Koech, D.; Liu, C.Y.; Aligui, G.; Gachihi, G.; Kombe, Y.; Parraga, I.; Ramirez, B.; Whalen, C.; Horton, R.J. and Reeve, P. (1999) Double-blind placebo-controlled study of concurrent administration of albendazole and praziquantel in schoolchildren with schistosomiasis and geohelminths. *The Journal of infectious diseases*, 179(4) 996–1003.

Olveda, D.U; Li, Y; Olveda, R.M; Lam, AK; Pchau,T.N; Ham, D.A. (2013) Bilharzia: Pathology, diagnosis, Management and Control.Tropical medicine and Surgery journal 2013

Oniya, M.O.; Ishola, M.A. and Jayeoba, O.D. (2013) Schistosomiasis in Ipogun : Update Assessment on Endemicity and Efficacy of Praziquantel in Chemotherapy. *International Journal of TROPICAL DISEASE & Health*, 3(1) 37–44.

Oniya, M.O. and Jeje, O. (2010) Urinary schistosomiasis : Efficacy of praziquantel and association of the ABO blood grouping in disease epidemiology. *International Journal for Biotechnology and Molecular Biology Reaearch*, 1(3) 31–35.

Ozowara, N.L.; Njoku, O.O.; Odikamnoro, O.O. and Uhuo, C. (2011) Study of the prevalence of Schistosoma haematobium infection and the treatment using praziquantel among school children in Ezza north local government area of Ebonyi state , Southeast Nigeria. *European Journal of Experimental Biology*, 1(2) 103–108.

Pax, R.; Bennett, J.L. and Fetterer, R. (1978) A Benzodiazepine Derivative and Praziquantel: Effects on Musculature of Schistosoma mansoni and Schistosoma japonicum. *Naunyn-Schmiedeberg's Archives of Pharmacology*, 304 309–315.

Pearce, E.J.; Kane, C.M.; Sun, J.; Taylor, J.J.; McKee, A.S. and Cervi, L. (2004) Th2 response polarization during infection with die helminth parasite Schistosoma mansoni. *Immunological Reviews*, 201 117–126.

Pereira, A.P.B.; Favre, T.C.; Galvão, A.F.; Beck, L.; Barbosa, C.S. and Pieri, O.S. (2010) The prevalence of schistosomiasis in school-aged children as an appropriate indicator of its prevalence in the community. *Memorias do Instituto Oswaldo Cruz*, 105(4) 563–569.

Peters, P.A.; El Alamy, M.; Warren, K.S. and Mahmoud, A.A.F. (1980) Quick Kato smear for field quantification of Schistosoma mansoni eggs. *American Journal of Tropical Medicine and Hygiene*, 29(2) 217–219.

Pfister, K.; Turner, K.; Currie, A.; Hall, E. and Jarrett, E.E.E. (1983) IgE production in rat fascioliasis. *Parasite Immunology*, 5(6) 587–593.

Pinot de Moira, A; Jones, F,M and Wilson, S.(2013) Effects of treatment on IgE responses against parasite allergen-like proteins and immunity to reinfection in childhood schistosome and hookworm coinfections. Infect Immun.

Pinot de Moira, A; Fulford, A.J; Kabatereine, N.B; Ouma, J.;, Booth, M. and Dunne DW.(2010) Analysis of complex patterns of human exposure and immunity to Schistosomiasis mansoni: the influence of age, sex, ethnicity and IgE. PLoS Negl Trop Dis.

Playfair, J.H.L. (1987) *Immunology at a glance*. 4th ed. Osney Mead, Oxford ; Malden, MA: Blackwell Science.

Racheal,LP; Jennifer LS; Rashmi S. and Simon Jb. (2014) Global numbers of infections and disease burden for soil transmitted helminth infections in 2010. BMC Parasites and Vectors

Remoue, F; To, Van, D; Schacht, A.M; Picquet, M. and Garraud O. (2001) Gender-dependent specific immune response during chronic human *Schistosomiasis haematobia*. Clin Exp Immunol

Richter J. (2003). The impact of chemotherapy on morbidity due to schistosomiasis. Acta Trop.

Roberts M, Butterworth AE, Kimani (1993). Immunity after treatment of human schistosomiasis: association between cellular responses and resistance to reinfection. Infect Immun.

Rodrigues, L.C.; Wheeler, J.G.; Shier, R.; Guerra, H.L.; Pimenta, F. and Lima eCosta, M.F. (2000) Predicting the community prevalence of schistosomiasis mansoni from the prevalence among 7- to 14-year-olds. *Parasitology*, 121 Pt 5 507–512.

Rihet, P; Demeure, C.E; Bourgois, A; Prata,A and Dessein, A,J. (1991) Evidence for an association between human resistance to *Schistosoma mansoni* and high anti-larval IgE levels. Eur J Immunol.

Rujeni, N.; Nausch, N.; Midzi, N.; Cowan, G.J.; Burchmore, R.; Cavanagh, D.R.; Taylor, D.W.; Mduluza, T. and Mutapi, F. (2013) Immunological consequences of antihelminthic treatment in preschool children exposed to urogenital schistosome infection. *Journal of Tropical Medicine*,.

Saathoff, E.; Olsen, A.; Kvalsvig, J.D. and Appleton, C.C. (2004) Patterns of geohelminth infection, impact of albendazole treatment and re-infection after treatment in schoolchildren from rural KwaZulu-Natal/South-Africa. *BMC infectious diseases*, 4(1) 27.

Sady, H.; Al-Mekhlafi, H.M.; Mahdy, M.A.K.; Lim, Y.A.L.; Mahmud, R. and Surin, J. (2013) Prevalence and Associated Factors of Schistosomiasis among Children in Yemen: Implications for an Effective Control Programme. *PLoS Neglected Tropical Diseases*, 7(8).

Sato, K.; Shimada, M.; Noda, S.; Muhoho, N.D.; Katsumata, T.; Sato, A. and Aoki, Y. (1988) Efficacy of metrifonate in a highly endemic area of urinary schistosomiasis in Kenya. *American Journal of Tropical Medicine and Hygiene*, 38(1) 81–85.

Satti, M.Z.; Lind, P.; Vennervald, B.J.; Sulaiman, S.M.; Daffalla, A.A.; Ghalib, H.W.; MZ, S.; Lind, P.; BJ, V.; SM, S.; AA, D. and HW, G. (1996) Specific immunoglobulin measurements related to exposure and resistance to Schistosoma mansoni infection in Sudanese canal cleaners. *Clin Exp Immunol*, 106(1) 45–54.

Scott, J.T; Turner, C.M; and Mutapi, F. (2000). Dissociation of interleukin-4 and interleukin-5 production following treatment for *Schistosoma haematobium* infection in humans. Parasite Immunol.

Senghor, B.; Diallo, A.; Sylla, S.N.; Doucouré, S.; Ndiath, M.O.; Gaayeb, L.; Djuikwo-Teukeng, F.F.; Bâ, C.T. and Sokhna, C. (2014) Prevalence and intensity of urinary schistosomiasis among school children in the district of Niakhar, region of Fatick, Senegal. *Parasites & vectors*, 7 5–5.

Senghor, B.; Diaw, O.T.; Doucoure, S.; Seye, M.; Diallo, A.; Talla, I.; B??, C.T. and Sokhna, C. (2016) Impact of Annual Praziquantel Treatment on Urogenital Schistosomiasis in a Seasonal Transmission Focus in Central Senegal. *PLoS Neglected Tropical Diseases*, 10(3) 1–17.

Senghor, B.; Diaw, O.T.; Doucoure, S.; Sylla, S.N.; Seye, M.; Talla, I.; Bâ, C.T.; Diallo, A. and Sokhna, C. (2015) Efficacy of praziquantel against urinary schistosomiasis and reinfection in Senegalese school children where there is a single well-defined transmission period. *Parasites & vectors*, 8(1) 362–362.

Seydel LS, Petelshi A, van Dam GJ, (2012). Association of *in utero* sensitization to *Schistosoma haematobium* with enhanced cord blood IgE and increased frequencies of CD5- B cells in African newborns. Am J Trop Med Hyg.

Silva, I.M. da; Thiengo, R.; Conceição, M.J.; Rey, L.; Lenzi, H.L.; Pereira Filho, E. and Ribeiro, P.C. (2005) Therapeutic failure of praziquantel in the treatment of *Schistosoma haematobium*

Shen, L; Zhang, Z.S and Wu,H.W. (2002) . Down-regulation of specific antigen-driven cytokine production in a population with endemic *Schistosoma japonicum* infection. Clin Exp Immunol. infection in Brazilians returning from Africa. *Memórias do Instituto Oswaldo Cruz*.

Siongok, T.K.A.; Mahmoud, A.A.F.; Ouma, J.H.; Warren, K.S.; Muller, A.S.; Handa, A.K. and Houser, H.B. (1976) Morbidity in Schistosomiasis Mansoni in Relation to Intensity of Infection: Study of a Community in Machakos, Kenya*. *The American Journal of Tropical Medicine and Hygiene*, 25(2) 273–284.

Siza, J.E.; Kaatano, G.M.; Chai, J.Y.; Eom, K.S.; Rim, H.J.; Yong, T.S.; Min, D.Y.; Chang, S.Y.; Ko, Y. and Changalucha, J.M. (2015) Prevalence of schistosomes and soil-transmitted helminths among schoolchildren in lake Victoria basin, Tanzania. *Korean Journal of Parasitology*, 53(5) 515–524.

Sutton, B.J. and Gould, H.J. (1993) The human IgE network. *Nature*, 366(6454) 421–8.

Taylor-Robinson, D.C.; Maayan, N.; Soares-Weiser, K.; Donegan, S. and Garner, P. (2015) Deworming drugs for soil-transmitted intestinal worms in children: effects on nutritional indicators, haemoglobin, and school performance. *The Cochrane database of systematic reviews*, (7) CD000371.

Thiong'o, F.W.; Mbugua, G.G.; Ouma, J.H. and Sturrock, R.K. (2002) Efficacy of oxamniquine and praziquantel in school children from two *Schistosoma mansoni* endemic areas. *East African Medical Journal*, 79(1) 29–33.

Traore, M.; Traore, H.A.; Kardorff, R.; Diarra, A.; Landoure, A.; Vester, U.; Doehring, E. and Bradley, D.J. (1998) The public health significance of urinary Schistosomiasis as a cause of morbidity in two districts in Mali. *American Journal of Tropical Medicine and Hygiene*, 59(3) 407–413.

Uneke, C.; Oyibo, P.; Ugwuoru, C.; Nwanokwai, A. and Iloegbunam, R. (2006) *Urinary Schistosomiasis Among School Age Children In Ebonyi State, Nigeria*. 2(1) 1–7.

UNESCO. Fresh tools for effective school health; Facts about Schistosomiasis

Verani, J.R.; Abudho, B.; Montgomery, S.P.; Mwinzi, P.N.M.; Shane, H.L.; Butler, S.E.; Karanja, D.M.S. and Secor, W.E. (2011) Schistosomiasis among young children in Usoma, Kenya. *American Journal of Tropical Medicine and Hygiene*, 84(5) 787–791.

Vereecken, K; Naus, C.W; and Polman, K. (2007) Associations between specific antibody responses and resistance to reinfection in a Senegalese population recently exposed to *Schistosoma mansoni*. Trop Med Int Health.

Verjovski-Almeida S; Leite LC; Dias-Neto E; Menck C,F; Wilson R,A.(2004) Schistosome transcriptome: insights and perspectives for functional genomics. Trends Parasitology

Walter, K.; Fulford, A.J.C.; McBeath, R.; Joseph, S.; Jones, F.M.; Kariuki, H.C.; Mwatha, J.K.; Kimani, G.; Kabatereine, N.B.; Vennervald, B.J.; Ouma, J.H. and Dunne, D.W. (2006) Increased human IgE induced by killing Schistosoma mansoni in vivo is associated with pretreatment Th2 cytokine responsiveness to worm antigens. *Journal of immunology (Baltimore, Md. : 1950)*, 177(8) 5490–8.

Warren, K.S. (1973)Regulation of the prevalence and intensity of schistosomiasis in man: immunology or ecology? J Infect Dis.

Watanabe, K.; Mwinzi, P.N.M.; Black, C.L.; Muok, E.M.O.; Karanja, D.M.S.; Secor, W.E. and Colley, D.G. (2007) T regulatory cell levels decrease in people infected with Schistosoma mansoni on effective treatment. *American Journal of Tropical Medicine and Hygiene*, 77(4) 676–682.

Watanabe, N.; Bruschi, F. and Korenaga, M. (2005) DOI: 10.1016/j.pt.2005.02.010 PMID: 15780839. *IgE: A question of protective immunity in Trichinella spiralis infection*. 4. Vol. 21.

Webster, M.; Correa-Oliveira, R.; Gazzinelli, G.; Viana, I.R.C.; Fraga, L.A.D.O.; Silveira, A.M.S. and Dunne, D.W. (1997) Factors Affecting High and Low Human IgE Responses to Schistosome Worm Antigens in an Area of Brazil Endemic for Schistosoma mansoni and Hookworm. *The American Journal of Tropical Medicine and Hygiene*, 57(4) 487–494.

Webster, M.; Fallon, P.G.; Fulford, A.J.C.; Butterworth, A.E.; Ouma, J.H.; Kimani, G. and Dunne, D.W. (1997) Effect of praziquantel and oxamniquine treatment on human isotype responses to Schistosoma mansoni: elevated IgE to adult worm. *Parasite Immunology*, 19(7) 333–335.

Webster, M.; Fulford, A.J.C.; Braun, G.; Ouma, J.H.; Kariuki, H.C.; Havercroft, J.C.; Gachuhi, K.; Sturrock, R.F.; Butterworth, A.E. and Dunne, D.W. (1996) Human immunoglobulin E responses to a recombinant 22.6-kilodalton antigen from Schistosoma mansoni adult worms are associated with low intensities of reinfection after treatment. *Infection and Immunity*, 64(10) 4042–4046.

Webster, M.; Libranda-Ramirez, B.D.L.; Aligui, G.D.; Olveda, R.M.; Oumsa, J.H.; Kariuki, H.C.; Kimani, G.; Olds, G.R.; Fulford, A.J.C.; Butterworth, A.E. and Dunne, D.W. (1997) The influence of sex and age on antibody isotype responses to Schistosoma mansoni and Schistosoma japonicum in human populations in Kenya and the Philippines. *Parasitology*, 114(4) 383–393.

WHO (2011) Helminth control in school-age children. A guide for managers of control programmes. *Geneva: World …*, 90–90.

WHO | Schistosomiasis (2015) Available from http://www.who.int/mediacentre/factsheets/fs115/en/

WHO-Soil-transmitted helminth infections (2014) Available from http://www.who.int/mediacentre/factsheets/fs366/en/

WHO – World Health Organization 2002. Prevention and control of schistosomiasis and the soil transmitted helminthiases. Report of WHO Expert Committee WHO Geneva.

Williams, M.E.; Montenegro, S.; Domingues, A.L.; Wynn, T.A.; Teixeira, K.; Mahanty, S.; Coutinho, A. and Sher, A. (1994) Leukocytes of Patients with Schistosoma mansoni Respond with a Th2 Pattern of Cytokine Production to Mitogen or Egg Antigens but with a Th0 Pattern to Worm Antigens. *The Journal of Infectious Diseases*, 170(4) 946–954.

. Wilson, S; Jones, F.M and Fofana, H.K, (2013).Rapidly boosted plasma IL-5 induced by treatment of human *Schistosomiasis haematobium* is dependent on antigen dose, IgE and eosinophils. PLoS Negl Trop Dis.

Winter, W.E.; Hardt, N.S. and Fuhrman, S. (2000) Immunoglobulin E: Importance in parasitic infections and hypersensitivity responses. *Archives of Pathology and Laboratory Medicine*, 124(9) 1382–1385.

Woolhouse, M.E. and Hagan, P. (1999) Seeking the ghost of worms past. *Nat Med*, 5(11) 1225–1227.

Woolhouse, M.E.J. (1998) Patterns in parasite epidemiology: The peak shift. *Parasitology Today*, 14(10) 428–434.

Woolhouse, M.E.J.; Taylor, P.; Matanhire, D. and Chandiwana, S.K. (1991) Acquired-Immunity and Epidemiology of Schistosoma-Haematobium. *Nature*, 351(6329) 757–759.

Worku, L.; Damte, D.; Endris, M.; Tesfa, H. and Aemero, M. (2014) Schistosoma mansoni infection and associated determinant factors among school children in Sanja Town, northwest Ethiopia. *Journal of Parasitology Research*, 2014(April).

Yami, A.; Mamo, Y. and Kebede, S. (2011) Prevalence and predictors of intestinal helminthiasis among school children in jimma zone; a cross-sectional study. *Ethiopian journal of health sciences*, 21(3) 167–74.

Zhao, F.; Huang, X. and Hou, X (2013). *Schistosoma japonicum*: susceptibility of neonate mice born to infected and noninfected mothers following subsequent challenge. Parasite Immunol.

Zhaosong, Z; Haiwei, W. and Suchen, C. (1997). Association between IgE antibody against soluble egg antigen and resistance to reinfection with *Schistosoma japonicum*. Trans R Soc Trop Med Hyg.

https://msu.edu/course/zol/316/alumgut.htm **:Life cycle of *Ascaris lumbricoides***

https://www.cdc.gov/parasites/trichuris/biology.html :Life cycle of *Trichuris trichura*

(https://medical-dictionary.thefreedictionary.com/hookworms:Life Cycle of Hookworm

APPENDICES

Appendix 1: WHO Intensity threshold of *S. mansoni*

Table 38: Intensity threshold of *S. mansoni*

S. mansoni	Intensity
Heavy	>400
Moderate	100-400
Light	<100

Appendix 2: WHO Intensity of *S. haematobium*

Table 39: Intensity threshold of *S. haematobium*

S. haematobium	Intensity
Heavy	>50
Light	<50

Appendix 3: Formula for Cure Rate and Egg Reduction Rate

Cure rate (CR) and Egg reduction rate (ERR)

$$CR = 1 - \left[No.infected\ post\ treatment \Big/ No.Infected\ pre\ treatment \right] \times 100$$

$$ERR = 1 - \left[Geometric\ mean\ of\ eggs\ post\ treatment \Big/ Geometric\ mean\ of\ eggs\ pre\ treatment \right] \times 100$$

Remarks

1) Interpretation: CR is the rate of those cured of the infection by the treatment while ERR is the rate at which the egg per 10ml of urine and eggs per gram of s.haematobium and *S. mansoni* respectively was reduced. Note that we used the Geometric mean.

2) 0% CR means no cure, 100% means a total elimination of the infection and a negative CR means there was reinfection cases.

0% ERR translates to no change in the geometric mean of the eggs, 100% ERR is the cases where the eggs were reduced to zero and a negative ERR means that there was an increase in the geometric mean of the eggs

Appendix 4: Formula for Risk Ratio and Odds Ratio

Risk Ratio & Odds Ratio: The probability of developing disease in an exposed group in comparison to a non-exposed group

The standard error and 95% confidence interval of risk ration are calculated according to Altman 1991

$$\mathbf{R.R}= \left[\frac{a}{a} + b \Big/ \frac{c}{c} + d \right]$$

Odds Ratio: Is a measure between an exposure and an outcome. It represents the odds that an outcome will occur given a particular exposure, compared to the odds of the outcome occurring in the absence of that exposure

The standard error and 95% confidence interval of odds ratio are calculated according to Altman 1991

$$\mathbf{OR}= \left[a/b \Big/ c/d \right]$$

Where:

In the case of comparison of groups (for example Schools)

Or in the case of comparison of periods (for example before and after treatment)

	Group 1	Group 2	Total
No. Positive	A	C	a+c
No. Negative	B	D	b+d
Total	a+b	c+d	a+b+c+d

Appendix 5: Data Collection Form for Child Information

CHILD INFORMATION	
Primary school code: |_____|_____|_____|_____|_____|_____|	**Primary school name:**
District Code: |____|____|____|	**District name:**
Child ID |____|____|____|____|____|____|____|____|____|____|	**Date of visit:** |____|____|/|____|____|/|____|____| ***day month year***
Student's last name	**Student's first name**
Student's initials	**Date of birth** |____|____|/|____|____|/|____|____| ***day month year*** 99/99/99=Not known
Age: |____|____| **years** **Class:** |____|____| **standard**	**Gender:** ☐**Male**☐**Female**
Parent/guardian's last name	**Parent/guardian's first name**

Appendix 6: Data collection form for school information

SCHOOL INFORMATION AND DEMOGRAPHICS	
Date of visit:|____|____|/|____|____|/|____|____| ***day month year***	
District name:	**District code:** |_____|_____|_____|
Name of school:	**School code:** |_____|_____|_____|
GPS Longitude: |___|___| : |___|___|___|___|___| E	**GPS Latitude**: |___|___| : |___|___|___|___|___| (N/S) Negative ☐ Positive☐(tick as appropriate)
School MoE code:	**Start of school term:**|____|____|/|____|____|/|____|____|
School type: Day ☐ Boarding☐	**Gender of pupils**: Mixed ☐ Boys☐ Girls ☐
Name of head teacher: **Name of second contact person (deputy head teacher or another teacher at school):**	**Head teacher phone number:** **Second contact phone number:**

A. SCHOOL DEMOGRAPHICS	**ECD**	**P1**	**P2**	**P3**	**P4**	**P5**	**P6**	**P7**	**P8**
A1.Total boys enrolled:									
A2. Total girls enrolled:									
A3. Total boys present today:									
A4. Total girls present today:									

A5. Total male teachers:	
A6. Total female teachers:	

WATER and SANITATION FACILITIES

B1. Does the school have any of the following? Ask to see.***Enter 1 =Yes and 2 = No***

Unlocked and accessible separate toilets for boys and girls .....

Hand washing facilities near the toilets .....

Water in handwashing facilities.....

Soap is available at the hand washing facility .....

Water available for drinking today .....

First Aid kit .....

If yes, what does it contain? [_____]

B2. What is the <u>main</u> source of water for drinking for students in this school?
Only enter one answer .....

1=Piped/tap water; 2=Borehole or well; 3=Rain water; 4=Stream or river; 5=Bought; 6=Bottled water;
7=Others.....*specify*[_____]

B3. How many months of the year does the school **not** have water available for pupils to drink? .....
No. months[__]

B4. What type of sanitary facilities does the school have?

Only enter one answer .....

1 = Water borne; 2 = VIP latrine; 3 = Ordinary latrine; 4 = Others (specify) [_____]

B5. Were the sanitary facilities cleaned today? .....

B6. How many latrine/toilet"seats" does the school have that are functional/currently in use on day of visit? (locked = unusable)

Total (should be total of all other rows) .....

ECD.....

Unassigned pupils .....

Boys only .....

Girls only.....

Teachersonly .....

B7. How many urinals are currently in use/functional?

Total .....

Unassigned pupils .....

Boys only .....

Girls only.....

B8. How many of those sanitary facilities (excluding urinals) have doors that close completely?

Unassigned pupils .....

Boys .....

Girls .....

B9. How many of those functional sanitary facilities (excluding urinals) have visible feces inside?

Unassigned pupils .....

Boys .....

Girls .....

B10. How many of those functional sanitary facilities (excluding urinals) have pits/tanks that are full?

Unassigned pupils .....

Boys .....

Girls .....

B11. How many of those functional sanitary facilities (excluding urinals) have excessive smell?

Unassigned pupils .....

Boys .....

Girls .....

B12. How many of those functional sanitary facilities (excluding urinals) have excessive flies?

Unassigned pupils .....

Boys .....

Girls .....

B13. How many of those functional sanitary facilities (excluding urinals) have a slab, walls and roof in good structural condition (no cracks)?

Unassigned pupils .....

Boys .....

Girls .....

B14. If the school has hand washing facilities near the toilets, what type are they?

Only enter one answer.....

1 = tap water; 2 = hand wash basin; 3 = leaky tins; 4 = Others (Specify) [_____

SCHOOL HEALTH ACTIVITIES and IEC MATERIAL

C1. In the last 12 months, was the school involved in any of the following school health activities? ***Enter 1 =Yes and 2 = No***

School feeding programme.....

If yes, is hand washing practiced before feeding? .....

Water and sanitation programme.....

School dewormingprogramme .....

If yes, who did the deworming [_____]

If yes, which deworming drugs were used: ☐Bilhazia/Schistosomiasis ☐ Lymphatic Filariasis☐ STH

Were any teachers at this school trained for school-based deworming in the past 6 months .....

If yes, who did the training [_____]

Any other programme, please specify
[_____]

Please provide details of the above programmes:

C2. Does the school have any of the following? ***Enter 1 =Yes and 2 = No***

Deworming IEC posters on display in the classrooms .....

Deworming IEC posters on display in the head teachers office .....

Deworming IEC booklets in the school library .....

Other deworming IEC material, please specify
[_____]

Please provide further details of the above:

Appendix 7: Deworming M & E post treatment

CHILD INFORMATION	
Primary school code: |_____|_____|_____|_____|_____||_____|	**Primary school name:**
District Code: [____]____]____]	**District name:**
Child ID |_____|_____|_____|_____|_____|____|____|____||_____|	**Date of visit:** |____|____|/|____|____|/|____|____| *day month year*
Student's last name	**Student's first name**
Student's initials	**Date of birth** |____|____|/|____|____|/|____|____| *day month year* 99/99/99=Not known
Age: |____|____| **years** **Class** |____|	**Gender:** ☐ **Male** ☐ **Female**
Parent/guardian's last name	**Parent/guardian's first name**

HEALTH INFORMATION	
Haemoglobin: |____|____|____| g/L	**Stool slide taken:** ☐ Yes ☐ No

SCHOOL FEEDING	
A1. Do you receive a hot lunch provided by the school? 1 = Yes; 2 = No; 3 = Don't know	☐ Yes ☐ No
A2 If Yes; for how long have you had a hot lunch?	1st Term 2012[__] 2nd Term 2012[__] 3rd Term 2012[__]
A3 Did you have a hot lunch in school yesterday? 1 = Yes; 2 = No; 3 = Don't know	☐ Yes ☐ No

DEWORMING USE
B1. Have you received treatment for worms in the last year?

Read out options, only enter one answer .....[__]

1 = Yes; 2 = No; 3 = Don't know

When was the treatment done, Date…….

B2. If yes, where did you receive treatment?

Read out options, only enter one answer .....[__]

1 = School**;** 2 = Health centre; 3 = Home; 4 = Community programme; 5 = Shop; 6= Others *specify* [_____]

B3 How many tablets? [__]

B4 Who gave you the tablet?

1= Teacher; 2= Nurse; 3=Parent 4= Community health worker [__]

B5. What colour were the tablets?

Enter one answer .....[__]

1 = White; 2 = Yellow; 3 = Blue; 4 = Others **…***specify* [_____]

Appendix 8: Blood collection process

Figure 15: Process of Blood collection

Appendix 9: Finger prick blood on Whatman filter paper

Figure 16: Finger prick blood on Whatman filter paper

Appendix 10: Elisa reader with microtiter plate

Figure 17: Elisa reader with microtiter plate

Appendix 11: Canal, water contact point

Figure 18: Canal, water contact point

Appendix 12: Children fetching water from a canal

Figure 19: Children fetching water from a canal

Appendix 13: Water contact

Figure 20: Water contact

Appendix 14: Children in school with and others without shoes

Figure 21: Children in school with and others without shoes

Appendix 15: Toilet facilities, with cemented floors

Figure 22: Toilet facilities, with cemented floors

Appendix 16: Hand washing facilities in the school

Figure 23: Hand washing facilities in the fchool