EPIDEMIOLOGY OF *SCHISTOSOMA HAEMATOBIUM* AND *SCHISTOSOMA MANSONI* INFECTIONS AMONG SCHOOL CHILDREN IN THE KASSENA/NANKANA WEST DISTRICT OF GHANA: PRE- AND POST- TREATMENT WITH PRAZIQUANTEL

A THESIS SUBMITTED IN
FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE OF

MASTER OF PHILOSOPHY

In the

Department of Clinical Microbiology
School of Medical Sciences

by

QUARSHIE YVONNE DZIFA

KWAME NKRUMAH UNIVERSITY OF SCIENCE & TECHNOLOGY,
KUMASI

FEBRUARY, 2012

DECLARATION

The experimental work described in this thesis was carried out at the Department of Clinical Microbiology, KNUST. This work has not been submitted for any other degree.

.....

Name of student

(Quarshie Yvonne Dzifa)

.....

Name of Supervisor

(Dr. Alexander Debrah)

.....

Head of Department

(Prof. E. H. Frimpong)

ABSTRACT

Schistosomiasis remains a public health problem and children are the most at risk of contracting the disease. It thus requires adequate treatment to avert irreversible future pathological conditions. Poverty and the lack of amenities make rural children the most vulnerable. This study assessed the prevalence rate, intensity and re-infection rates of *S. haematobium* and *S. mansoni* among school children in the Kassena/Nankana West District pre- and post-treatment with standard dose of praziquantel. The levels of exposure to infection risk factors were also assessed with the use of a structured questionnaire.

A randomized intervention study was conducted in the Kassena/Nankana West District between April 2010 and August 2011 comprising a total of 239 school children. The children were made up of 137 males and 102 females with ages ranging between 6 and 17 years. Demographic, behavioral and symptomatic details were recorded using a questionnaire. Urine and stool samples were collected from the same children pre- and post-treatment for parasitological examinations. Infected children received a single dose of 40 mg/kg body weight praziquantel and its effectiveness was followed up at 24 and 48 weeks post-treatment.

Initial prevalence of *Schistosoma haematobium* and *Schistosoma mansoni* infections was 10.9% and 28.0% respectively. The prevalence of both infections peaked in the 11-15 years age group and was higher in males. For treated *S. haematobium* infected children, re-infection rate was 16.7% at 24 weeks and 42.9% at 48 weeks; intensity reduction rate at 24 weeks was 58.8% and 79.4% at 48 weeks. For treated *S. mansoni* infected children, re-infection rate was 12.5% at 24 weeks and 14.3% at 48 weeks; intensity reduction rate was 38.5% at 24 weeks and relatively poor (-73.9%) at 48 weeks. Univariate risk factors for *S. haematobium* were males (cOR = 3.4, p = 0.018), reports of bloody urine (cOR = 3.0, p= 0.012) and farm work (cOR = 0.2, p = 0.011); and for *S. mansoni*, males (cOR = 5.0, p = <0.0001), contact with water bodies (cOR = 4.5, p = 0.016), ever been treated for schistosomiasis (cOR = 2.5, p = 0.014) and farm work (cOR = 0.2, p=0.027). Sex adjusted risks for *S. haematobium*, were farm work (cOR = 0.2, p = 0.040) and bloody urine (cOR = 2.5, p = 0.037); and for *S. mansoni*, age (cOR = 0.9, p = 0.038) and ever been treated (cOR = 2.4, p = 0.031). Thus, a two dose regimen of praziquantel will be beneficial for children in the Kassena/Nankana West District.

ACKNOWLEDGEMENT

For the lord is a faithful God. Blessed are those who wait for his help (Isaiah 30: 18b).

And whatever you do or say, do it as a representative of the lord Jesus, giving thanks through him to God the father (Colossians 3 : 17) .

I am grateful to God for the abundant grace and favor, strength and travelling mercies He showed me throughout this research.

My heartfelt gratitude goes to:

My husband, Mr. Martin Quarshie who supported me financially and emotionally and showed me lots of love and encouragement that kept me going. I am blessed to have you by my side.

My parents, Dr. and Mrs. Aklaku, for their immense help and encouragement and for taking care of my children whenever I was away. We are blessed to still have you around.

My able supervisor, Dr. Alexander Debrah, whose advice, patience, sacrifice and support contributed tremendously to the success of this work. It was indeed a pleasure having you as my mentor.

The Chiefs, District Director of Education for Kassena/Nankana West, Heads, Teachers and Children of Katiu, Nyagnia and Kayoro E/A primary schools for their warm reception and various contributions to the success of this research.

My senior colleagues, Mr. Albano Bayita of Tamale Central Laboratory, Mr. Lawrence Yelifari of Bolga Regional Laboratory and Mr. Philip Amati of Navrongo War Memorial Hospital Laboratory for their collaboration and for sharing their knowledge, expertise, advice and support in time of need. I count myself privileged.

Dr. Patrick Ansah and Mr. Victor Asoala of the Navrongo Research Centre, for their selfless support which made this work a success. God bless you.

Mr. Nii Teiko Quaye of NewLife Laboratory and Clinic for immensely and selflessly contributing his knowledge in statistics and general thesis writing to this work. Your support is priceless.

The field staff, Hamza Adam, Enock Nii Bortier Angenu and Abdul Aziz Billa, for your diligence, energy, loyalty and sacrifice. It was pleasant working with you.

To everyone who contributed to this work in one way or the other, I say thank you and God richly bless you for obeying Romans 12 : 13; ***when God's people are in need, be ready to help them. Always be eager to practice hospitality.***

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

Chapter 1

INTRODUCTION

1.1 GENERAL INTRODUCTION

Schistosomiasis also known as bilharziasis is a chronic infection of the circulatory system caused by parasitic helminths that inflame mainly the intestines, bladder, and liver (Dunne *et al.*, 1995). There are five species of the genus *Schistosoma* that affect humans; *Schistosoma haematobium*, which migrates to the perivesical and periureteral vessels, *S. mansoni* to the inferior mesenteric, *S. japonicum* to the superior mesenteric and two others, *S. intercalatum* and *S. mekongi,* to both mesenteric vessels (Goldsmid *et al.*, 1998).

Schistosomiasis is endemic in over 74 developing countries, affecting more than 200 million people and causing more than 300 000 deaths per year in Sub-Saharan Africa alone (van der Werf *et al.*, 2003). The disease is contracted from waterborne cercaria of the parasite that penetrate the skin and enter the bloodstream where they develop, pair, and reach sexual maturity (King, 2009). Parasite transmission and the consequent risk of human infection are strongly linked to specific geographical locations (King, 2009). This is because the parasite goes through several developmental stages that must occur in fresh water, including a period of growth within particular species of intermediate host snails. Factors responsible for the increasing incidence of schistosomiasis in the Weija lake basin include immigration of disease-infected fishermen and peasant farmers, flaws in resettlement programmes, changes in the flow rate of water and proliferation of water weeds (Ampofo and Zuta, 1996). Other activities such as swimming in water bodies, dry season activity of irrigation, fetching water and mixing clay for moulding blocks and earthen ware (utensils) increase rate of infection (Ampofo and Zuta, 1996).

Schistosomiasis is a disease of chronic inflammation that substantially affects the daily performance of the millions of people who are or have been infected. The response of the host to schistosomes or their eggs results in different pathologies including dermatitis, granulomas and fibrosis (Boyd, 1995).

Schistosomiasis remains one of the world's most prevalent and neglected tropical diseases and it is the commonest cause of haematuria worldwide which is associated with disabling anaemia and malnutrition as well as poor performance in school and at work (Boyd, 1995). Schistosome pathogenesis can be grouped into acute and chronic schistosomiasis. Schistosomiasis often remains undiagnosed thereby leading to the chronic stage which presents more severe pathological conditions after prolonged infection. Thus, posing a serious threat to the health status of infected individuals, especially to children who live along the banks of aquatic intermediate snail host infested large fresh water reservoirs and frequently come in contact with infested waters. Besides symptoms of acute infections which are easier to detect in an infected individual, other chronic conditions such as glomerulopathy, rectal prolapse, fibrosis, hepatosplenic diseases, liver cirrhosis and cancer among others are more life threatening and can be avoided if infections are detected earlier and measures are taken to avoid progression to the chronic and mostly irreversible stages.

Eukaryotic pathogens, such as schistosomes, with complex life cycles expose their hosts to discrete life stages that express different subsets of genes, thus to differing sets of antigens. In response to these antigens, the host develops certain immunological mechanisms which are directed against worm antigens or against egg antigens, depending on the stage of infection (Grzych *et al.*, 1991; Pearce *et al.*, 1991). These immunogens may comprise

cellular, humoral or innate immunity which are important in limiting infection. A complex array of both humoral and cellular immune responses develops in patients with schistosomiasis to soluble cercaria, worm and egg antigens. However, only the egg antigens are important in the pathogenesis of complex inflammatory responses (granulomas) (Ogunba *et al.*, 1982). The granulomatous pathway to schistosoma eggs belongs to the "hypersensitivity" granuloma category which responds to antigens and usually requires T-cell sensitization in an attempt to wall off, contain and perhaps, destroy the tissue deposited around schistosome ova (Arinola, 2005). The highly efficient process of cellular influx to inflammatory sites is mediated by a plethora of mediator substances supporting and dispersing inflammation (Ibelgauft, 2008). These mediators which are found in the serum or tissue fluids, are released by degranulating cells, and are secreted also by inflammatory cells upon activation, or activated endothelial cells in blood vessels at the site of inflammation (Ibelgauft, 2008).

The treatment of choice for all schistosome species is praziquantel (Biltricide®) (Ross *et al.*, 2002). Praziquantel is extremely well-tolerated and is used both for treatment of individual patients and in mass community treatment programs (WHO, 1993). A standard single oral dose of 40mg/kg body weight is the current dosage for human schistosomiasis due to its successful activity as a single dose against all schistosome species and the absence of severe side effects (WHO, 1985). Its use in the field generally results in cure rates of 80% to 95% with a reduction rate in those not cured of 90% to 95% for *S. haematobium* and more than 60% with egg reduction rates of 90%-95% in those not cured for *S.* mansoni infections one year after the dose (WHO, 1985; Davis, 1993). Poor treatment outcomes have however been observed in certain areas, increasing concerns that resistance

has emerged, or will soon emerge, as seen in other human parasites (Davis and Wegner, 1979; Brindley, 1994).

1.2 AIM

In this study, the epidemiology of schistosomiasis and the effectiveness of praziquantel which is the drug of choice for treatment of *S. haematobium* and *S. mansoni* are assessed before and after treatment, among school children in the Kassena/Nankana West District.

1.3 SPECIFIC OBJECTIVES

1. To estimate the prevalence rate and intensity of schistosomiasis among school children in the Kassena/Nankana West District pre- and post-treatment with praziquantel.
2. To assess re-infection rates of *S. haematobium* and *S. mansoni* among school-age children after treatment with standard dose of praziquantel.
3. To assess the level of exposure of the school children to infection risk factors by questionnaire administration.

1.4 JUSTIFICATION OF THE PROJECT

Schistosomiasis, although an endemic disease in Ghana often remains undiagnosed thereby leading to more severe pathological conditions after prolonged infection. This poses a serious threat to the health status of infected individuals, especially to children who live along the banks of snail infested large fresh water reservoirs.

Besides haematuria and bloody diarrhoea which are easier to detect in infected individuals, other conditions such as chronic renal failure, rectal prolapse, cancer, intestinal and hepatosplenic diseases among others are more life threatening and can be avoided if infections are detected earlier and the appropriate treatment regimen given to avoid progression to chronic and mostly irreversible stages. Reports have suggested that praziquantel is not always effective, pointing to the possible development of resistant strains in countries like Senegal (Fallon *et al.*, 1995). Mass drug administration (MDA) to all school children in schistosomiasis endemic areas will soon be embarked upon by WHO and UNICEF together with governments of endemic countries. However, it is not clear whether the current dose of 40 mg/kg body weight is effective in clearing the parasite. Therefore, it is imperative that a small pilot work is carried out to ascertain the effectiveness of the dosage intended for the MDA. Knowledge of the prevalence, incidence and the re-infection rates associated with praziquantel treatment will therefore give an idea of the dosage and how often treatment should be administered to control schistosomiasis infection especially in children in the absence of a vaccine.

It is in light of this that this research was undertaken to assess the effectiveness of praziquantel, the drug of choice for the treatment of schistosomiasis in the

Kassena/Nankana West District. This would be a stepping- stone to the need for implementing preventive measures against the debilitating effect of schistosomiasis through chemotherapy.

Chapter 2

LITERATURE REVIEW

2.1 HISTORY AND EPIDEMIOLOGY

Schistosomiasis, also called bilharziasis is a parasitic disease that leads to chronic ill health.

It is one of the world's oldest helminth diseases which have been recognized since the time of the Egyptian Pharaohs. The worms responsible for the disease were discovered in 1851 by Theodor Bilharz (Bilharz, 1852) , a young German pathologist from whom the disease took its original name, Bilharziasis.

Schistosomiasis is the second most common parasitic disease after malaria in socioeconomic and public health importance in tropical and subtropical areas (Doumenge *et al.*, 1987). Schistosomiasis is now endemic in 74 countries and territories throughout the world. It affects 200 million individuals worldwide, causing between 500,000 and 800,000 deaths per year (Hunter *et al.*, 1993; Bergquist, 1998). About 779 million people are estimated to be at risk of schistosomiasis, of whom 106 million (13.6%) live in irrigation sites or in close proximity to large dam reservoirs (Steinmann *et al.*, 2006). In Sub-Sahara Africa, it has been estimated that urinary schistosomiasis cause haematuria in 70 million people and bladder pathology in 18 million individuals (van der Werf *et al.*, 2003).

Of the 16 species of schistosomes known to infect man and animals, *S. mansoni* and *S. haematobium* are the endemic species in Ghana (Doumenge *et al.*, 1987). Data dating back to 1970's indicated that urinary schistosomiasis is widespread in all parts of the country and intestinal schistosomiasis is restricted and patchy in its distribution; highly endemic within settlements located along river bodies in all the ten regions of Ghana (MOH-GHS, 2007-2008). Many water development projects, such as Lake Volta and Lake Kpong, the Tono

irrigation project, the Weija dam and other small water projects throughout the country, have resulted in new foci of transmission throughout the county. The prevalence of *S. haematobium* increased from 5- 10% to 90% in the Volta basin after the construction of the Akosombo dam on the river Volta (WHO, 1993). In response to population pressures and seasonal hunger in the North Eastern part of Ghana between 1958 and 1960, 104 small dams were constructed which tripled the prevalence of *S. haematobium* from 17% to 51% in 38 survey areas (Hunter *et al.*, 1993).

Factors affecting the epidemiology of schistosomiasis include epidemiological diversity, physical environment, water resource development, human ecology, population movement and transportation (Doumenge *et al.*, 1987).

2.2 SCHISTOSOMA SPECIES

2.2.1 *Schistosoma haematobium*

This species has a terminal- spined egg and causes urinary schistosomiasis. Isolates of *S. haematobium* from Africa and adjacent regions can display many differences in infectivity to various species of the snail genus *Bulinus* (Doumenge *et al.*, 1987). The peak prevalence and intensity of infection for *S. haematobium* occurs in children aged between 10 and 14 years with low prevalence and intensity in the older age group (Doumenge *et al.*, 1987).

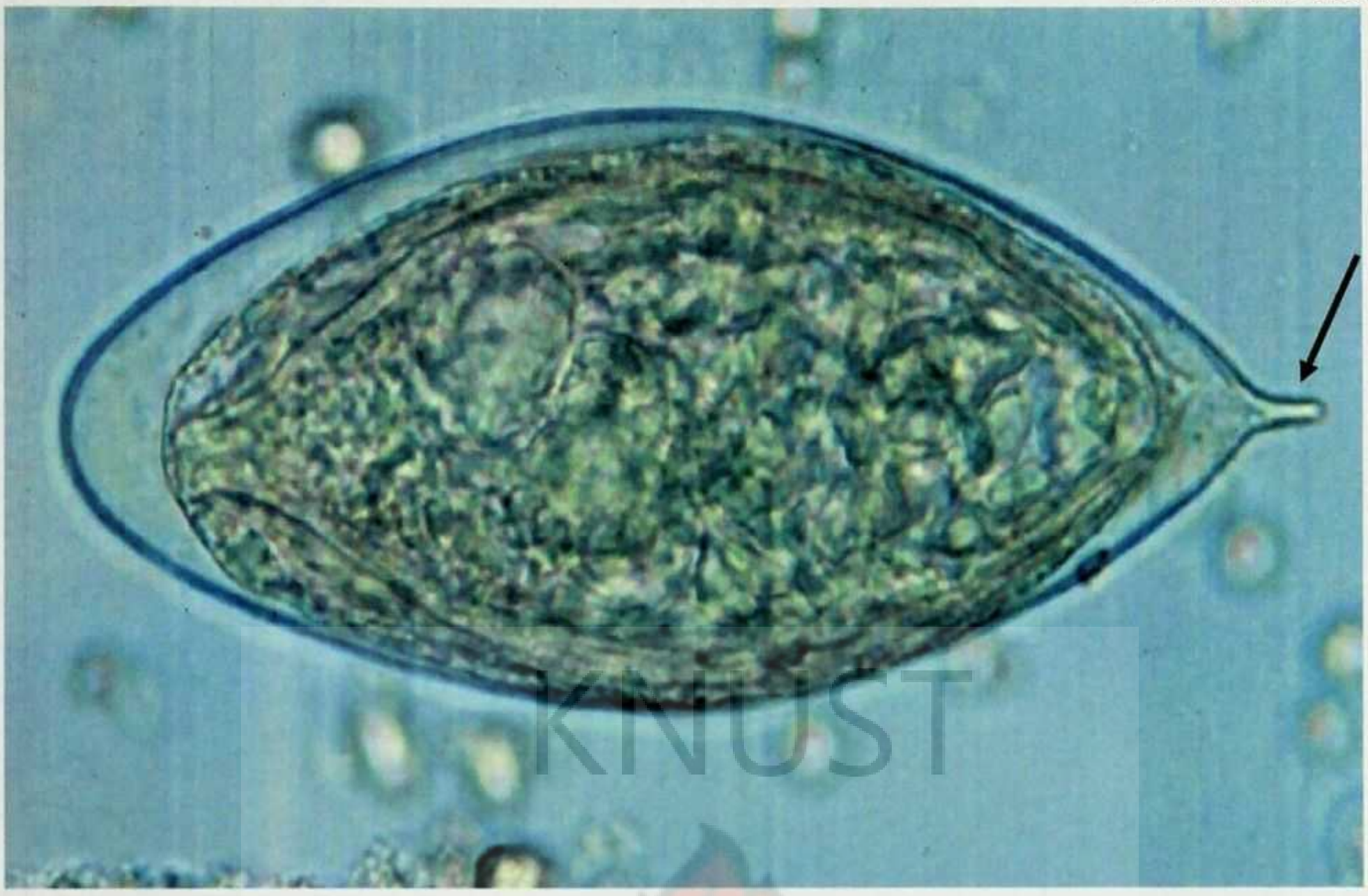

Figure 2.1 Egg of *S. haematobium* in wet mount of urine concentrate, showing characteristic terminal spine (arrowed).

(source:http://www.dpd.cdc.gov/dpdx/IMAGES/ParasiteImages/SZ/schistosomiasis)

2.2.2 *Schistosoma mansoni*

This species of schistosomes causes intestinal schistosomiasis. It is the only species with a lateral - spined egg that infects humans. Isolates of *S. mansoni* from different geographical areas show many differences in their ability to develop in the various species and strains of the snail genus *Biomphalaria* (Doumenge *et al.*, 1987). The age-group between 10-24 years in endemic areas show the greatest prevalence of *S. mansoni* infection with children between the ages of 10 and 14 years being the most heavily infected (Doumenge *et al.*, 1987).

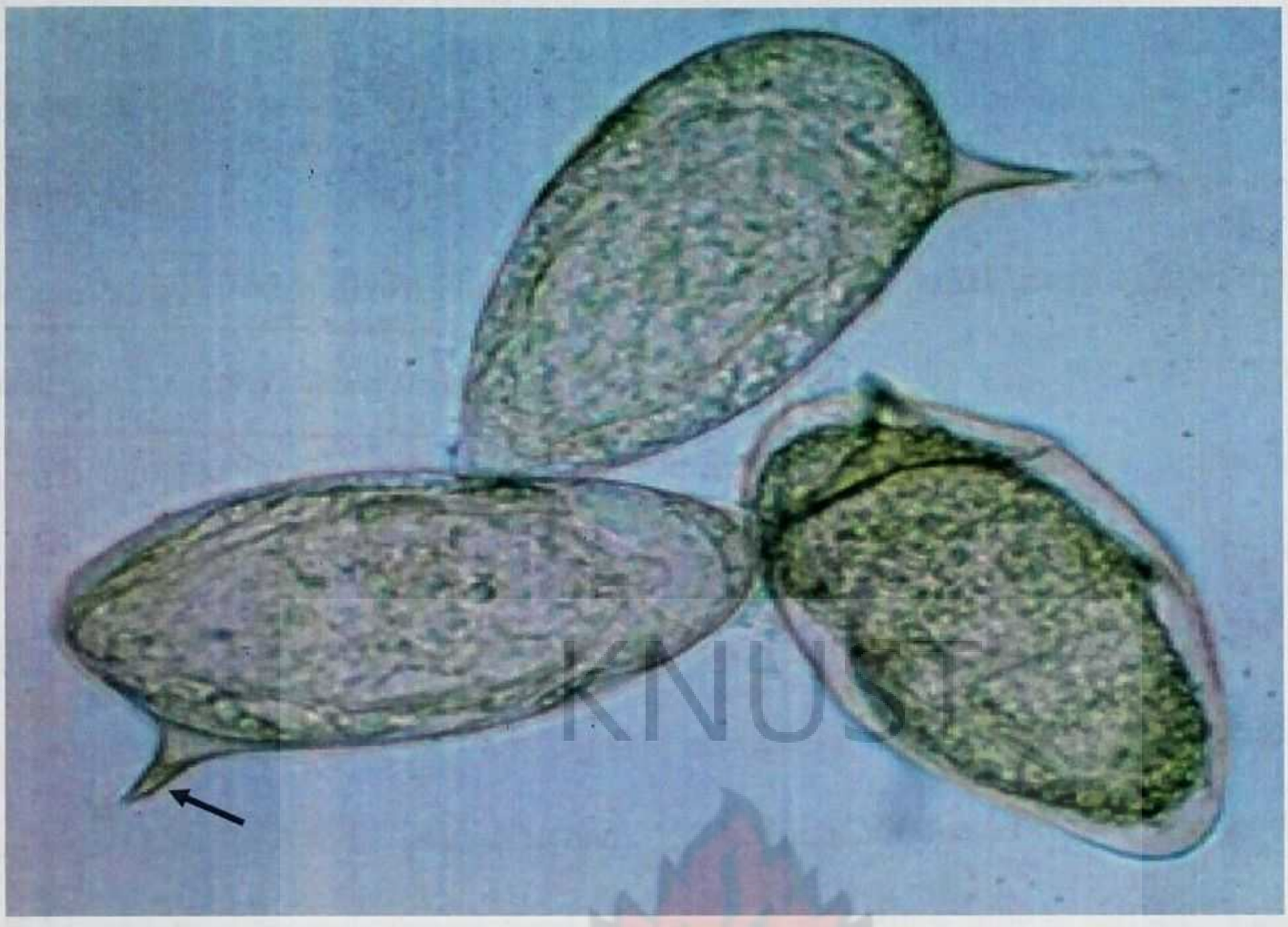

Figure 2.2 Eggs of S. *mansoni* in unstained wet mount showing prominent lateral spine (arrowed).
(source: http://www.dpd.cdc.gov/dpdx/IMAGES/ParasiteImages/S-Z/schistosomiasis)

2.3 TRANSMISSION AND LIFE CYCLE OF SCHISTOSOMES

Transmission of *Schistosoma* species occurs by cercaria penetrating the skin when a person baths, washes clothes, fishes, swims, or engages in agricultural work or other activities involving contact with cercaria infested water (Cheesbrough, 1999). *Shistosoma* species have an indirect life cycle. Humans are the most significant definitive hosts. Intermediate hosts of *Schistosoma* species are aquatic snails; *Biomphalaria* species for *S. mansoni* and *Bulinus* species for *S. haematobium*. In Ghana, the disease is transmitted by *Bulinus rholfsi* and *Bulinus globosus* (Odei, 1995). They are found on vegetation in ponds, streams, rivers, lakes, dams, irrigation channels and in rice paddies. After penetration of the skin, the cercariae lose their tails and develop into schistosomula which migrate via the lungs to the liver. In the portal venous system, the schistosomulae become mature flukes over a period

of up to four weeks and pair. Adult male and female schistosomes mate in the liver and then migrate as pairs against blood flow to their final niche in the mesenteric plexus (the destination for *S. mansoni*) or the venous plexus of the bladder (the destination of *S. haematobium*) (Boyd, 1995). Four to eight weeks after the initial penetration of the skin by cercariae, the adult females begin laying eggs. Many of the eggs penetrate through the mucosa into the lumen of the bladder (*S. haematobium)* or intestine (*S. mansoni)* where they are excreted about 12 weeks after infection (Cheesbrough, 1999). Eggs trapped in the bladder or intestine incites a granulomatous reaction, and the eggs die and calcify. By a variety of mechanisms the worm is capable of evading the host immune response and can live in the host for 5 to 10 years (Damian, 1984). Eggs eliminated from the body that reach suitable fresh water conditions hatch to releases miracidia which actively search for a suitable snail host to infect. The miracidia enter the snail through the head and/or foot and undergo a process of multiplication and development in the digestive gland of the snail. This stage of the life cycle in the snail takes 4-6 weeks. One snail can release up to 300 cercariae per day, each capable of infecting a single person. Cercariae remain viable in fresh water for up to 48 hours during which time they may successfully penetrate exposed skin.

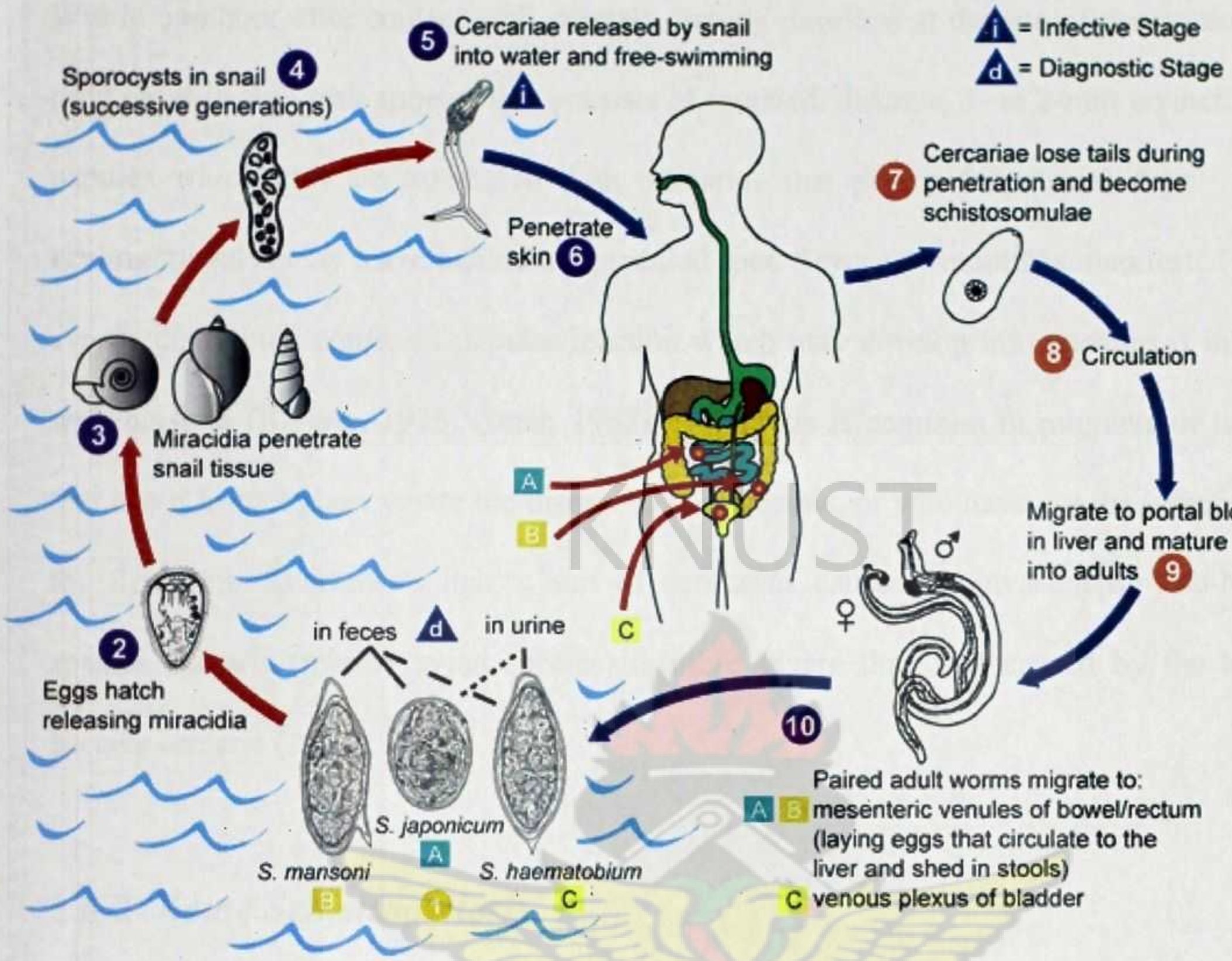

Figure 2.3 Life Cycles of *Schistosoma* species
(source: http://en.wikipedia.org/wiki/File:Schistosomiasis_Life_Cycle.jpeg)

2.4 PATHOGENESIS OF SCHISTOSOMES

The response of the host to schistosomes or their eggs results in different pathologies. Each species may give rise to acute or chronic disease with widely differing symptoms and clinical signs which can be categorized into; dermatitis, acute schistosomiasis and chronic schistosomiasis (Chen and Mott, 1989).

2.4.1 *Dermatitis*

Within one hour after contact with cercaria, itching develops at the site of penetration. In mild cases, a skin rash appears that consists of rounded, discrete, 1- to 2-mm erythematous papules which may be associated with urticariae that persist for several days. Upon healing, papules may leave behind a pigmented spot. Severe dermatitis is manifested by an evenly distributed confluent papular reaction which may develop into pustules if infected with bacteria (Barlow, 1936; Amer, 1982). Dermatitis is common in migrants or tourists that come from a place where the disease is not endemic, or who have got the infection for the first time. Swimmer's itch, a sort of dermatitis caused by invasion by non-human species cercaria (mainly avian species) is more severe than that caused by the human species cercaria (Amer, 1982).

2.4.2 *Acute Schistosomiasis*

Symptoms of acute infection appear four to ten weeks after heavy exposure to cercariae and present as a clinical syndrome often seen in non-immune individuals (tourists, immigrants, or the indigenous population) who have been exposed in an endemic area to a primary infection (Boyd, 1995). The syndrome also referred to as Katayama fever is a severe disease; however, the mechanism involved in its clinical manifestation is not completely understood. Both non-immune and immune mechanisms may participate in the pathogenetic process. In the early stages of infection with *S. haematobium*, the acute granulomatous response to parasite eggs causes urinary tract diseases, such as bladder polyposis and urothelial ulceration which in turn causes urinary frequency, dysuria and end stream haematuria (WHO, 1993; Paul *et al.*, 2002). Haematuria may also result when terminal-spined eggs clog the venous plexus, impeding blood flow thus causing the veins to

burst, allowing blood and eggs to enter the urinary bladder (WHO, 1985). In a study conducted by de Jesus *et al.,* (2002) involving 31 patients with acute schistosomiasis due to *S. mansoni*, symptoms such as malaise, headache, myalgia, edema, and abdominal pain as well as major organ involvement, such as liver and spleen enlargement, elevated liver enzymes, pericarditis, and restrictive respiratory insufficiency were observed. Symptoms of the acute stage are transient and spontaneously disappear with the passage of the infection to the chronic stage.

The acute disease rarely appears in people residing where schistosomiasis is endemic, suggesting that the adaptive immune response protects them from developing the acute toxemic condition presumably because of their pre-and postnatal exposures to schistosome antigens via transplacental, lactation, and repeated infections at an early age (Santoro *et al.*, 1977; Carlier *et al.*, 1980). This view is supported by murine experiments in which foetal or neonatal exposure to schistosome antigens induced a state of hypo-responsiveness and diminished the granulomatous responses of adult animals (Lewert and Mandlowitz, 1969; Hang *et al.*, 1974).

2.4.3 *Chronic Schistosomiasis*

This stage of infection is believed to begin 10 weeks and above after infection. A general relationship between intensity of infection and morbidity in children has been confirmed in a review study of morbidity caused by chronic schistosomiasis by Chen and Mott (1989). Antigens released by the maturing ova stimulate a local inflammatory response that facilitates their passage from within the vein into the liver in hepatic schistosomiasis and in the bladder lumen in urinary schistosomiasis or the intestinal wall in intestinal

schistosomiasis (Doenhoff *et al.*, 1978). Many eggs lodge in the definitive hosts' liver and intestine or bladder, where they elicit a cellular granulomatous reaction that, with its ensuing fibrosis, gives rise to the most serious symptoms of chronic infections (Dunne *et al.*, 1995). The severity and nature of granulomatous inflammation is an important risk factor for development of morbidity (Warren, 1982).

Chronic *S. mansoni* infections are associated with intestinal and hepatosplenic diseases. The principal intestinal lesions are colonic polyposis, focal fibrosis and inflammation (WHO, 1993). During the intestinal phase of the disease, which may begin a few months after the infection and may last for years, symptomatic patients characteristically display colicky abdominal pains and bloody diarrhoea (Mahmoud, 2001). The hepatosplenic phase may manifest early, during the first year of infection particularly in children. WHO (1993) reported that a correlation between hepatomegaly in childhood and intensity of infection has been established in endemic communities. Reversible hepatosplenomegaly may occur in early infestations not complicated by the development of portal hypertension and is usually, but not invariably, associated with enlargement of the liver and spleen (De Cock, 1986). In subsequent phases of infection, presinusoidal blockage of blood flow leads to portal hypertension and splenomegaly (Mahmoud, 2001). Portal hypertension might lead to varices at the lower end of the esophagus and at other sites. Bleeding from esophageal varices may, however, be the first clinical manifestations of this phase, and patients may experience repeated bleeding. In the last stage of the disease, typical fibrotic changes occur along with liver function deterioration and the onset of ascites, hypoalbuminaemia and defects in coagulation (Mahmoud, 2001). The liver may gradually decrease in size, but increases in hardness as fibrosis is gradually extended into the parenchyma, resulting

eventually in liver cirrhosis in severe cases. The enlarged spleen may reach the level of the umbilicus or even at times expand to fill most of the abdomen (De Cock, 1986). Features of hepatocellular failure, ascites often being the most obvious clinical sign, may complicate the end stage hepatosplenic schistosomiasis. Nutritional deficiencies and concurrent viral infections of the liver may as well accelerate or exacerbate the deterioration of hepatic function. In chronic diseases associated with *S. haematobium*, ureteric and bladder fibrosis and calcification are more common in older patients. At this stage, urinary egg count is less related to severity of the disease. Obstructive uropathy and squamous cancers resulting from bladder lesions may later develop (Dunne *et al.*, 1995).

2.5 IMMUNOPATHOLOGY OF SCHISTOSOMES

Field studies in endemic areas, combined with animal experiments, have led to the view that host genetics, infection intensity, *in utero* sensitization to schistosome antigen and co-infection status all influence the development of the immune response and, so, disease severity (Pearce and MacDonald, 2002).

In the case of *S. mansoni* infection, hepatic periportal fibrosis, hepatosplenomegaly, and portal hypertension are the major causes of schistosomiasis morbidity and mortality (Bonnard *et al.*, 2004). The most serious effects of infection with *S. haematobium* are bladder cancer (Ishii *et al.*, 1994) and genital schistosomiasis, a condition in which eggs pass through the cervix in women or into the testes in men (Feldmeier *et al.*, 1999; Poggensee *et al.*, 2001).

2.5.1 *Egg Induced Granulomas*

Granulomas are complex inflammatory responses against materials that are retained in tissues often for prolonged periods of time. They are often classified as "hypersensitivity" - type granulomas or" foreign body"- type granulomas, of which pathology to shistosome eggs belongs. Schistosomal egg granuloma, a cell mediated type of immunologic response is the main pathologic feature in schistosomiasis (Arinola, 2005). Granuloma formation is initiated by antigens secreted by the miracidium through microscopic pores within the rigid egg shell, and there is strong evidence that the vigorous granulomatous response, rather than the direct action of parasite egg antigens is responsible for the pathologic tissue manifestations in schistosomiasis (Boros, 1989). Some authors have established through early studies using experimental mice that, eggs released in the acute phase of the disease elicit vigorous granuloma formation whiles granulomatous response to those released at subsequent times is diminished (Andrade, 1964; Boros *et al.*, 1975). This spontaneous down-regulation has been termed "immuno-modulation" of which failure to occur has been linked in humans to the development of severe forms of the disease.

Egg induced granulomas in *S. mansoni* and *S. Japonicum* infections result from trapping of the many eggs that are carried by blood flow into the liver. The sinusoids are too small for the eggs to traverse and thus become a dead-end for eggs which eventually die within the tissue. Eggs traversing through the intestine can also cause intestinal damage. In *S. haematobium* infections, egg passage across the bladder also cause damage to this organ. Egg antigens orchestrate a CD4+ T-cell response leading to the formation of an intense granulomatous reaction, composed of lymphocytes, macrophages and a large number of eosinophils, around eggs deposited in the tissues (Dunne and Pearce, 1999; Davies and

McKerrow, 2001). These reactions progress to fibrosis, leading to portal hypertension, with hepatosplenomegaly in the case of *S. mansoni* and *S. japonicum* and various urinary tract manifestations in the case of *S. haematobium* (Butterworth, 1998).

2.5.2 *Hepatic Fibrosis*

Fibrosis enhances the disease pathology and contributes to the mortality of *S. mansoni*. It follows the granulomatous inflammatory response (Dunn and Kamel, 1981; Wyler, 1983; Phillips and Lammie, 1986; Boros, 1987; Grimaud, 1987) and occurs mostly at the site of the resolving granulomatous reactions. However, fibrous bands also appear around portal veins distant from granulomas. At least two different cell types initiate hepatic granuloma fibrosis in humans: fibroblasts and the smooth-muscle cells that differentiate to myofibroblasts (Grimaud, 1987). It appears that both host immune and parasite factors are involved in triggering fibroblast activation and collagen synthesis. Fibroblasts secrete extracellular matrix proteins (ECMP) that deposit in the periportal space following immune modulated granulomas (Mahmoud, 2001). In most infected subjects living in endemic areas, ECMP accumulation is well controlled, and these individuals develop minor pathological manifestations. However, in 5–10% of *S. mansoni* infected subjects, ECMP accumulate in the portal space, due to imbalance between fibrogenesis and fibrolysis, leading to extended periportal fibrosis (PPF), also called Symmers' pipestem fibrosis. PPF is a major cause of portal hypertension and its attendant sequel, which include varices and abdominal ascites (Mahmoud, 2001). IL-1, IL-4, IL- 13, IL-7, TNF-α, monocyte chemo tactic protein1 (MCP-1), platelets derived growth factors (PDGF), and transforming growth factor-beta (TGF-β) stimulate the production of collagen and ECMP. It was realized in a study conducted by Hood and Boros (1980), that mice splenectomized at the height of the

granulomatous response responded with enlarged granulomas, but increase in granuloma size left total liver collagen content unchanged. Thus, a direct relationship between granuloma size and the degree of fibrosis could not be established.

2.5.3 *Glomerulopathy*

The urogenital system is the primary target of *S. haematobium* and occasionally *S. mansoni* infestation (Barsoum, 1993). The main initial lesions are found in the urinary bladder, in the form of "pseudotubercles," polyps and ulcers. As these lesions heal, they lead to a wide spectrum of diffuse bladder pathology including "sandy patches," chronic cystitis, bladder calcification, "cystitis cystica" and others (Badr, 1986). There is evidence that some of these lesions may predispose to malignancy, villous squamous cell carcinoma of the bladder being classically linked with schistosomiasis (Ishak, 1967). Variations have been detected in clinically overt lower and upper urinary tract pathologies in various studies which have been linked to ecological factors including differences in parasitic strains (Taylor *et al.*, 1973), intensity of infection (Cheever *et al.*, 1975; Warren *et al.*, 1979; Masaba *et al.*, 1983) and host susceptibility (Bina *et al.*, 1978).

Several histopathological classifications of glomerular pathology have been described with schistosomiasis. The most common by far is mesangioproliferative also known as class I. It is the earliest of *S*chistosoma associated lesions in experimental animals (De Brito *et al.*, 1971; Hillyer and Lewert, 1974). Together with 1gM and C3, schistosomal worm antigen mesangial deposits are most often encountered in this Class. The exudative (class II) type has been described mainly in patients with hepatosplenic schistosomiasis complicated by *Salmonella* infection (Bassily *et al.*, 1976; Salih *et al.*, 1977; Lambertrucci *et al.*, 1988). As

the name implies, the basic glomerular pathology is acute inflammatory, with many neutrophils, monocytes, blood platelets and a lot of fibrin amidst the proliferating endocapillary cells (Bassily *et al.*, 1976). Class III (Mesangiocapillary (membranoproliferative) glomerulonephritis (MCGN), has been reported as one of the types of glomerular diseases associated with *S. haematobium* glomerulopathy (Ezzat *et al.*, 1978). The prevalence of this pattern among asymptomatic patients with *S. mansoni* hepato-intestinal disease is low, varying between 6.7% and 20% (Rocha *et al.*, 1976; Barsoum, 1992), compared with up to 80% in those with overt renal disease. The identity of Class IV: Focal and segmental sclerosis (FSGS) as one of the patterns of schistosomal glomerulopathy is supported by experimental models in hamsters (Hillyer and Lewert, 1974) and baboons (Brack *et al.*, 1972; Houba, 1979).

Schistosoma associated amyloidosis (Class IV) is not species-dependent. It has been noticed with almost equal frequency among patients with *S. mansoni* and *S. haematobium* infestations (Barsoum, 1993), and prognosis is poor. Specific parasite antigens mediate the initial glomerular injury in schistosomal glomerulopathy. Soluble egg (Houba *et al.*, 1977) and tegument (Moriearty and Brito, 1977) antigens have been detected in certain studies. However, worm antigens have been incriminated in the vast majority as circulating antigens in infested patients (Capron *et al.*, 1965; Carlier *et al.*, 1975; Madwar and Voller, 1975; Brito *et al.*, 1979), as well as in experimentally infected animals (Natali and Cioli, 1974; Digeon *et al.*, 1979; Deelder *et al.*, 1980). Specific antibodies of all major immunoglobulin classes have also been detected in the sera of infested patients (Jassim *et al.*, 1987). Hepatic fibrosis is a common factor associated with the evolution of glomerular lesions. In most animal models, liver fibrosis usually precedes (Natali and Cioli, 1974; Van March *et al.*,

1977) and often correlates (Von Lichtenberg *et al.*, 1971; Brack *et al.*, 1972) with the glomerular lesions. Even with *S. haematobium* associated glomerulopathy, hepatic fibrosis has been reported as a prerequisite for the development of glomerular lesions in mice (Cheever *et al.*, 1983).

2.6 PREVENTION AND CONTROL OF SCHISTOSOMIASIS

The occurrence of Schistosomiasis is intimately related to the conditions of poverty and associated with poor hygiene, lack of safe water and of adequate sanitation particularly in developing countries. Many control programmes have been, and continue to be successful in reducing mortality, morbidity, and transmission (WHO, 2002).

WHO (2002) recommends a strategy for morbidity control as the first objective to reduce the consequences of early morbidity associated with *Schistosoma* infection, as well as late stage chronic and irreversible sequalae to a level that no longer constitutes a public health burden. This involves the administration of effective, safe, and inexpensive single-dose drugs. A more permanent approach to schistosomiasis control can however be achieved by the provision of safe water supply, coupled with construction of footbridges across infested rivers and streams, the provision of safe recreational bathing sites, especially for children and the protection of water supplies from faecal pollution by animal reservoir hosts by providing sanitation facilities in the communities (Cheesbrough, 1999).

The high risk groups for schistosomiasis such as school-age children, women of child bearing age and people whose occupations involve contact with infested water (fishermen, farmers, irrigation workers and women in their domestic task) can be reached through health and education systems- with extended community-based coverage where populations

are severely affected (WHO, 2002). Environmental measures such as application of molluscicides, where this is affordable and feasible and will not harm important animal and plant life, removing vegetation from locally used water places, draining swamps, and environmental measures to prevent seasonal flooding which results in an increase in snail numbers and transmission among other measures can be applied to destroy snail intermediate hosts (Cheesbrough, 1999).

2.7 PRAZIQUANTEL THERAPY

Praziquantel has a wide range of activity against trematodes and cestodes and is widely used in schistosomiasis as well as other fluke infections. It is currently the drug of choice for the treatment of human schistosomiasis and is extremely well-tolerated and widely used both for treatment of individual patients and in mass community treatment programs (WHO, 1993). Praziquantel was discovered in the 1970s and introduced in clinical practice in the early 1980s under the trade name Biltricide. When administered it is rapidly metabolized by humans to an inactive form which is excreted through the urine opposed to schistosomes which are incapable of transforming it metabolically (Andrews, 1981). Its mechanism is based on an induction of ultra structural changes in the teguments of adult worms, resulting in increased permeability to calcium ions (Brindley and Sher, 1990). Calcium ions accumulate in the parasite cytosol, leading to muscular contractions and ultimate paralysis of adult worms. By damaging the tegument membrane, praziquantel also exposes parasite antigens to host immune responses. These effects lead to dislodgement of worms from their intestinal sites and subsequent expulsion by peristalsis.

The manufactures recommend a dose of 20 mg/kg body-weight given three times in one day for all schistosomal infections. However, (WHO, 1985) recommended doses are a

single dose of 40 mg per kg body-weight for *S. haematobium*, *S. intercalatum*, or *S. mansoni* infection; up to 60 mg per kg body-weight in some areas for *S. mansoni* or mixed infections; or two doses of 30 mg per kg body-weight given with a 4-hour interval for *S. japonicum* infections. Its use in the field generally results in cure rates of 80% to 95% with a reduction rate in those not cured of 90% to 95% for *S. haematobium* and > 60% with egg reduction rates of 90%-95% in those not cured for *S. mansoni* infections one year after the dose (WHO, 1985; Davis, 1993).

Like all antihelminthics at standard dose, praziquantel may not kill 100% of adult worms *in vivo* (Andrews, 1981). Though very effective it may produce lower cure rates than expected resulting from a number of factors including pre-treatment intensity of infection, diagnostic sensitivity and age of the treated individual, poor patient compliance and timing at which treatment is evaluated (Andrews, 1985; Sabah *et al.*, 1986; Shaw, 1990; Scherrer *et al.*, 2009). Xiao *et al.*, (1985) explained that the immature forms of schistosome in the peripheral systemic circulation are apparently resistant to the standard dose of praziquantel than the more mature parasites located in the liver or mesenteric veins due to the lower/non-lethal concentrations of unchanged praziquantel in the peripheral systemic circulation. Even though re-infection may occur soon after treatment, particularly in children, pathology is resolved or at least its development is delayed (Mohamed-Ali *et al.*, 1991; Doehring-Schwerdtfeger *et al.*, 1992; WHO, 1993).

Side effects with praziquantel may be common but they are usually mild and transient. Frequent reports include headache, dizziness, drowsiness, abdominal discomfort, and nausea. Allergic- type reactions such as fever, urticaria, and pruritic skin rashes may occur due to death of the infecting parasites (Martindale, 1993)

Chapter 3

MATERIALS AND METHODS

3.1 STUDY AREA

The study was carried out in the Kassena/Nankana West district of the Upper East region.

The area is surrounded with many water bodies such as dams, including the Tono dam, rivers and streams. These water bodies serve as sources of water for various activities including drinking, washing, bathing/swimming, irrigation (Tono irrigation scheme), among others. Agriculture (fishing and irrigation farming) is the major occupation and source of economic survival of residents in the area. Children were recruited from the Katiu, Nyangnia and Kayoro Primary Schools. The selection of the area was based on reports on the prevalence of schistosomiasis among inhabitants from hospitals, clinics and research centres in the area.

Figure 3.1 Kassena/Nankana District showing the major villages

3.2 STUDY DESIGN

Prior to the commencement of the research, ethical approval was sought from the Committee on Human Research, Publication and Ethics of Kwame Nkrumah University of Science and Technology and the Komfo Anokye Teaching Hospital, Kumasi, Ghana. Formal notification of intent to conduct the study in Katiu, Nyagnia and Kayoro primary schools was given to the heads of all the institutions and the District Director of Education Kassena/Nankana West for which approval was duly given. Student participation in the study was voluntary and given the age of the study participants, consent for participation in the study was sought from parents/guardians who signed on behalf of their wards. The study was conducted between April, 2010 and August, 2011. All children with approved consent to participate in the study answered a self-structured questionnaire. Stool and urine samples were then obtained from the qualified children, examined for schistosome eggs and analyzed. All participating children were categorised into infected and not infected. The infected category was then split randomly by sequential numbering into infected and treated and infected and not treated groups (controls). Children in the infected and treated group were given a single oral dose of 40mg/kg body weight praziquantel (WHO, 1993). Follow-up sampling and testing of urine and stool were conducted 24 weeks and 48 weeks after the initial treatment of the children.

3.3 STUDY POPULATION

The study population comprised of children in grades 1-6 who were within the age group of 6-17 years and who at the time of the study were respective candidates of the schools

3.3.1 *Inclusion Criteria*

All children between the ages of 6 -17 years whose guardian/parent signed consent forms (Appendix 1), qualified after answering a questionnaire and agreed to produce urine and stool samples were included in the study. All children who provided a urine specimen during the pre-treatment survey were included at each follow-up time point

3.3.2 *Exclusion Criteria*

All children treated or on treatment with a schistosomicide in the past two years were exempted from the study. However, children who refused to participate or who were absent or unable to produce a specimen during each of the follow-up visits were not included in the analysis of the respective surveys.

3.4 SAMPLE SIZE CALCULATION

The sample size was estimated using the Cochran formular (1963) as follows:

$$N = \frac{Z^2\, pq}{d^2}$$

Where:

N = sample size

Z = abscissa of the normal curve that cuts off an area α at the tails (1- α equals the desired confidence level at 95%

d = desired level of precision (5%)

p = estimated proportion of an attribute present in a population

q = 1 – p

From available literature, estimated proportion of 34.4% has been stated in a study in Cape Coast (Okanla *et al.*, 2003) with proportional ranges of 2% - 31% being reported in different communities along the lower Volta river basin (Nkegbe, 2010).

Taking the average of the least and highest quoted proportions, the average estimated proportions used in this study was:

$$\frac{2\% + 34.4\%}{2} = 18.2\%$$

With: Z = 1.96, d = 5% (0.05), p = 18.2% (0.182) and q = 0.818

$$N = \frac{(1.96)^2(0.182)(0.818)}{(0.05)^2}$$

$$N = \frac{0.572}{0.0025}$$

$$N = 228.8 \cong 229$$

The minimum estimated sample size is 229, however, to factor for attrition rate and loss to follow up, the overall sample size was adjusted to 240.

3.5 SAMPLE COLLECTION, DIAGNOSIS AND QUANTIFICATION OF EGGS

3.5.1 *S. haematobium*

Urine samples were collected between 10:00 hrs and 14:00 hrs. Participating children were given a labeled 20 ml capacity wide mouthed, leak-proof container and asked to provide urine specimen. Filled specimen containers were brought to the laboratory where filtration of a sub-sample of 10mls was carried out on the same day. Eggs were recovered from urine

by using the filtration technique, which is a sensitive, rapid and reproducible technique for detecting and quantifying *S. haematobium* eggs in urine. Using blunt-ended forceps, a polycarbonate membrane filter (Whatman nucleopore^{R}) was carefully placed on the filter support of the filter holder. Holding the syringe over a beaker, 10mls of urine was slowly passed through the filter membrane. The filter holder was unscrewed and the blunt forceps was used to carefully remove and transfer the filter to a slide. Using the 10× objective with the condenser iris closed sufficiently to give good contrast, the entire filter was examined systematically for *S. haematobium* eggs. The number of eggs were counted and reported as number of eggs per 10mls of urine. Specimens of less than 10 ml were measured before filtration and the number of eggs per 10 ml calculated. Geometric mean egg count (GMEC), intensity reduction rate and re-infection rate were estimated as follows:

$$Geometric\ mean\ egg\ count$$
$$= antilog(mean\ of\ all\ log\ trasformed\ egg\ counts) + 1$$

$$Intensity\ reduction\ rate = \left[1 - \left(\frac{GMEC\ per\ 10\ mL\ urine\ after\ treatment}{GMEC\ per\ 10\ mL\ urine\ before\ treatment}\right)\right] \times 100$$

$$Re - Infection\ rate = \left(\frac{Number\ infected\ in\ treated\ group}{Number\ treated\ and\ present\ at\ follow - up}\right) \times 100$$

3.5.2 *S. mansoni*

Participating children were given a labeled wide mouthed, leak-proof container and asked to provide a specimen of faeces. The specimen containers were brought to the laboratory where eggs were recovered from the faeces by the Kato-Katz technique (Katz *et al.*, 1972). Faeces were pressed through a mesh screen with pore size of 200µm to remove large particles. A template with a hole of 25mg capacity was placed on a slide and filled with a small amount of the sieved faecal material. The template was then removed and the sample was covered with a piece of cellophane pre-soaked in glycerol-malachite green solution. Pressure was applied on the cellophane to spread the sample out on the slide. Using the 10× objective with the condenser iris closed sufficiently for good contrast, the entire area on the slide covered with faeces was examined systematically. The number of eggs counted in 25mg of faeces was multiplied by 40 to give the number of eggs per gram of faeces (epg). Geometric mean egg count (GMEC) of all individuals was used to assess average egg counts, intensity reduction rate was calculated on the basis of geometric mean to assess the percentage at which egg loads were reduced in the treated group and re-infection rate to assess the percentage of re-infected children in the treated groups as follows:

$$Geometric\ mean\ egg\ count$$

$$= antilog(mean\ of\ all\ log\ trasformed\ egg\ counts) + 1$$

$$Intensity\ reduction\ rate$$

$$= \left[1 - \left(\frac{GMEC\ per\ gram\ of\ stool\ after\ treatment}{GMEC\ per\ gram\ of\ stool\ before\ treatment}\right)\right] \times 100$$

$$Re - Infection\ rate = \left(\frac{Number\ infected\ in\ treated\ group}{Number\ treated\ and\ present\ at\ follow-up}\right) \times 100$$

3.6 PRAZIQUANTEL ADMINISTRATION

Children who were eligible for treatment included those between the ages of 6 years and 17 years who were infected with either/both *Schistosoma spp* by microscopy. Children who had been treated for schistosomiasis within the past two years, and those who chose to withdraw were excluded from the treatment group. Before the administration of praziquantel, each child who was eligible for treatment was given a roll of bread to eat after which a number of tablets corresponding to 40 mg/kg body weight as was indicated on a dosing sheet was administered. The children were asked to swallow the tablets with water under direct observation in order to monitor adherence. Arrangements were made with a Medical Doctor at the Navrongo research centre to attend to children who reported of adverse effects.

3.7 QUESTIONNAIRE ADMINISTRATION

Children in the selected schools were briefed on schistosomiasis. All children who showed interest in participating in the study were given a questionnaire to fill with the help of the teachers and the research team. Demographic, behavioral and symptomatic details were collated, indicating among others the children's contact with water bodies, activities they carry out around the water bodies, whether they had ever been treated for schistosomiasis, when last they were treated, symptoms of body weakness and the presence or absence of blood in their urine and stool (Appendix 1).

3.8 STATISTICAL ANALYSIS

Continuous data are presented as means ± SD and categorical data are presented as proportions. Student's *t*-test was used to test the statistical significance of all continuous variables and the Chi-square test statistic was used to test the statistical significance of all categorical variables. Logistic regression was used to test the association between variables associated with risk of *S. haematobium* and *S. mansoni* infections. For all comparisons, a p value <0.05 was considered to be statistically significant. Geometric mean egg count (GMEC) was calculated because the egg counts were not normally distributed.

Chapter 4

RESULTS

The general characteristics of the study population stratified by study site are presented in table 4.1. Out of a total of 239 subjects recruited for the study, 95 (39.7%) were from Katiu, 110 (46.0%) were from Nyagnia and 34 (14.2%) were from Kayoro. The age range of participants from Katiu was 6-17 years, Nyagnia 7-17 years and Kayoro 9-17 years. Analysis of age and weight of the subjects showed children from Kayoro were significantly older (14.2 ± 3.1 years) ($p < 0.0001$) and heavier (38.6 ± 8.0 kg) ($p < 0.0001$) than their counterparts from Nyagnia (11.6 ± 2.8 years, 31.1 ± 8.8 kg) and Katiu (11.6 ± 2.7 years, 29.4 ± 6.7 kg). The number of males in Nyagnia (68.2%) was significantly more than the number of males in Katiu (44.2%) ($p = 0.0005$) while a comparison of the number of males in Katiu and Kayoro (58.8%) and Nyagnia and Kayoro showed no statistically significant differences.

Table 4.1 Demographic comparison by study site

Data are presented as means ± SD and proportions. p^a defines the level of significance when Katiu was compared to Nyagnia; p^b defines the level of significance when Katiu was compared to Kayoro; p^c defines the level of significance when Nyagnia was compared to Kayoro

	Study Site					
Variables	**Katiu (n = 95)**	**Nyagnia (n = 110)**	**Kayoro (n = 34)**	**p^a**	**p^b**	**p^c**
Age (years)	11.6 ± 2.7	11.6 ± 2.8	14.2 ± 3.1	0.9261	<0.0001	<0.0001
Weight (kg)	29.4 ± 6.7	31.1 ± 8.8	38.6 ± 8.0	0.1362	<0.0001	<0.0001
Sex						
Male (%)	42(44.2)	75(68.2)	20(58.8)	0.0005	0.1433	0.3141
Female (%)	53(55.7)	35(31.8)	14(41.2)			

4.1 SCHISTOSOMIASIS PREVALENCE IN THE STUDY SITES

The overall pre-treatment infection prevalence of *S. haematobium* and *S. mansoni* in the three study sites was 10.9% (26/239) and 28.0% (67/239) respectively, including 6.3% (15/239) with both infections. An assessment of infection prevalence showed 17.6% (6/34) of the subjects in Kayoro having significantly higher *S. haematobium* infection compared to 1.1% (1/95) in Katiu ($p = 0.0002$) and 3.6% (4/110) in Nyagnia ($p = 0.005$). Subjects in Katiu had significantly higher *S. mansoni* infection of 24.2% (23/95) when compared to subjects from Kayoro with 2.9% (1/34) ($p = 0.0062$) who when compared to subjects from Nyagnia with 25.5% (28/110) had significantly lower *S. mansoni* infection ($p = 0.0042$). There were significantly more subjects with mixed infections in Nyagnia (12.7%; 14/110) compared to subjects from Katiu ($p = 0.0003$) and Kayoro ($p = 0.1025$) (Table 4.2).

Table 4.2 Prevalence rates for *S. haematobium* and *S. mansoni* by site

	Study Site					
Type of infection	Katiu (n=95)	Nyagnia (n=110)	Kayoro (n=34)	p^a	p^b	p^c
S. haematobium	1(1.1)	4(3.6)	6(17.6)	0.2317	0.0002	0.0050
S. mansoni	23(24.2)	28(25.5)	1(2.9)	0.8372	0.0062	0.0042
Mixed	0(0)	14(12.7)	1(2.9)	0.0003	0.0933	0.1025

Data are presented proportions. p^a defines the level of significance when Katiu was compared to Nyagnia; p^b defines the level of significance when Katiu was compared to Kayoro; p^c defines the level of significance when Nyagnia was compared to Kayoro

4.2 PREVALENCE OF *S. HAEMATOBIUM* INFECTION BY SEX AND AGE GROUP

Out of a total of 93 infected children, 26 children were infected with *S. haematobium*, of which 34.6% (9/26) fell within the 6 – 10 years age group, 66.7% (6/9) being males and 33.3% (3/9) females. Sixteen (61.5%) children fell within the 11 – 15 years age group of which 87.5% (14/16) were males and 12.5% (2/16) were females. No *S. haematobium* infection was observed in children above 15 years of age (Figure 4.1).

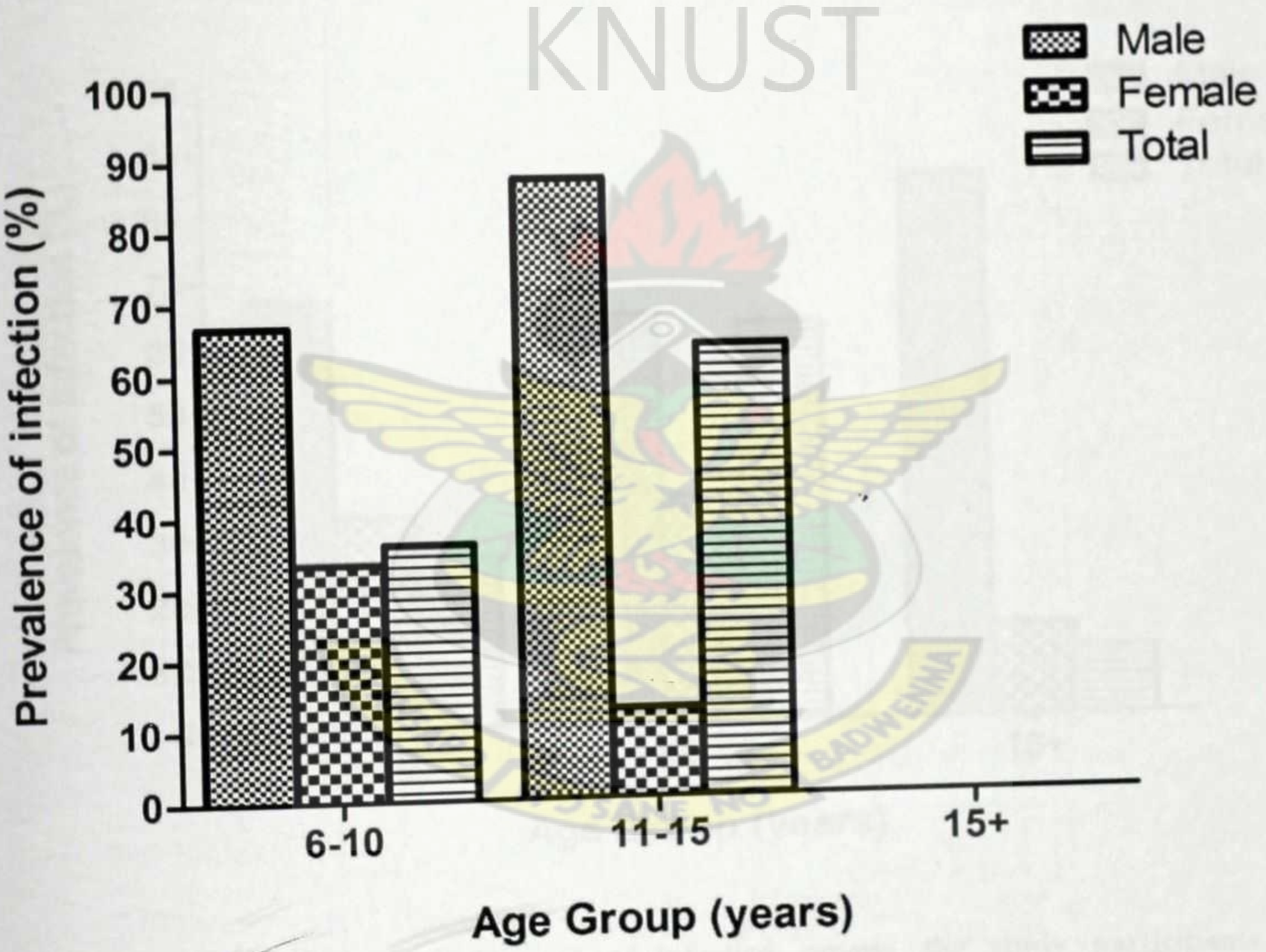

Figure 4.1 Prevalence of *S. haematobium* infection among the study participants categorized by age groups

4.3 PREVALENCE OF *S. MANSONI* INFECTION BY SEX AND AGE GROUPS

Out of a total of 67 *S. mansoni* infected children, 26.9% (18/67) were within the 6-10 years groups. Of this, 66.7% (12/18) were males and 33.3% (6/18) were females. Forty-two (62.7%) fell within the 11 – 15 years age group out of which 64.3% (27/42) were males and 35.7% (15/42) were females. Within the greater than 15 years age group, 10.4% (7/67) were infected with *S. mansoni* of which 85.7% (6/7) were males and 14.3% (1/7) were females (Figure 4.2).

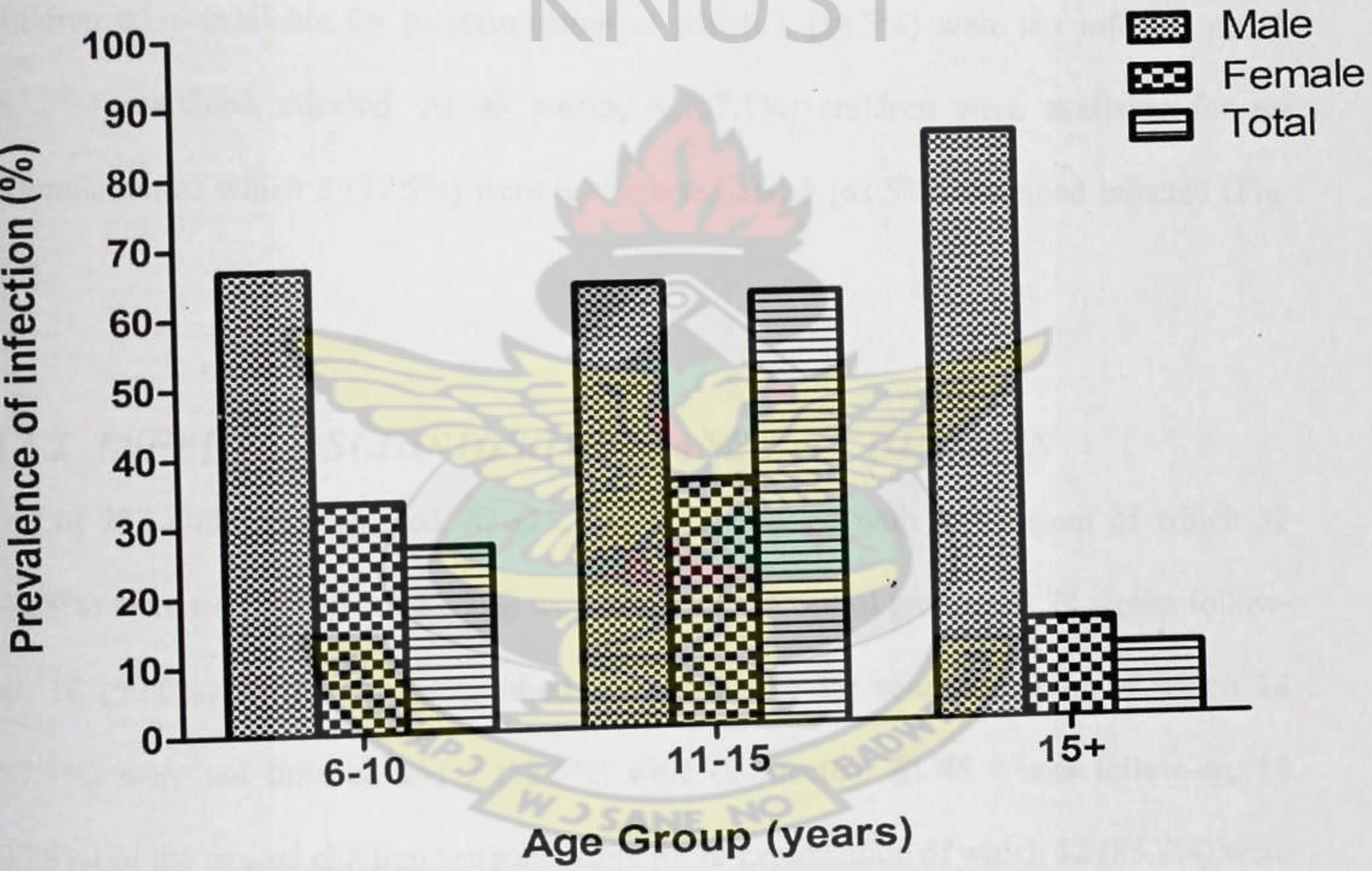

Figure 4.2 Prevalence of *S. mansoni* infection among the study participants categorized by age groups

4.4 TREATMENT OF INFECTED CHILDREN WITH PRAZIQUANTEL

4.4.1 *INFECTED SCHISTOSOMA HAEMATOBIUM CHILDREN*

Out of 224 children examined, 26 (11.6%) were infected with *S. haematobium* of which 12 (46.2%) were treated and the other 14 (53.8%) were not treated. At 24 weeks follow-up, 6 (50%) of the treated children were available for re-examination of which 5 (83.3%) were not infected and 1 (16.7%) was re-infected. At 48 weeks follow-up, 7 (58.3%) of the treated children were available for re-examination of which 4 (57.1%) were not infected and 3 (42.9%) were re-infected. For the positive control group, at 24 weeks follow-up, 6 (42.9%) children were available for re-examination of which 1 (16.7%) were not infected and 5 (83.3%) remained infected. At 48 weeks, 8 (57.1%) children were available for re-examination of which 3 (37.5%) were not infected and 5 (62.5%) remained infected (Fig. 4.3).

4.4.2 *INFECTED SCHISTOSOMA MANSONI CHILDREN*

Out of 232 children examined, 67 (28.9%) were infected with *S. mansoni* of which 32 (47.8%) were treated and 35 (52.2%) were not treated (control group). At 24 weeks follow-up, 16 (50.0%) of the treated children were available for re-examination of which 14 (87.5%) were not infected and 2 (12.5%) were re-infected. At 48 weeks follow-up, 14 (43.8%) of the treated children were available for re-examination of which 12 (85.7%) were not infected and 2 (14.3%) were re- infected. For the control group, at 24 weeks follow-up, 20 (57.1%) children were available for re-examination of which 5 (25.0%) were not infected and 15 (75.0%) remained infected. At 48 weeks, 19 (54.3%) children were available for re-examination of which 26.3% (5) were not infected and 73.7% (14) remained infected (Fig. 4.4).

4.4.3 *NON-INFECTED SCHISTOSOMA HAEMATOBIUM CHILDREN*

Out of an initial number of 224 children tested, 199 (88.8%) were not initially infected with *S. haematobium*. At 24 weeks follow-up 132 out of 199 children not infected were available for re-examination of which 122 (92.4%) remained non-infected whiles 10 (7.6%) were newly infected. At 48 weeks follow-up, 56.3% (112/199) of the children were available for re-examination of which 100 (89.3%) were non-infected whiles 12 (10.7%) were newly infected (Fig 4.5).

4.4.4 *NON-INFECTED SCHISTOSOMA MANSONI CHILDREN*

Out of an initial number of 232 children tested, 166 (71.6%) were initially not infected with *S. mansoni.* At 24 weeks follow-up 112 out of 166 were available for re-examination of which 93 (83.0%) were still not infected whiles 19 (17.0%) were newly infected. At 48 weeks follow-up, 56.0% (93/166) of the children were available for re-examination of which 79 (84.9%) were still not infected whiles 14 (15.1%) were newly infected (Fig. 4.6).

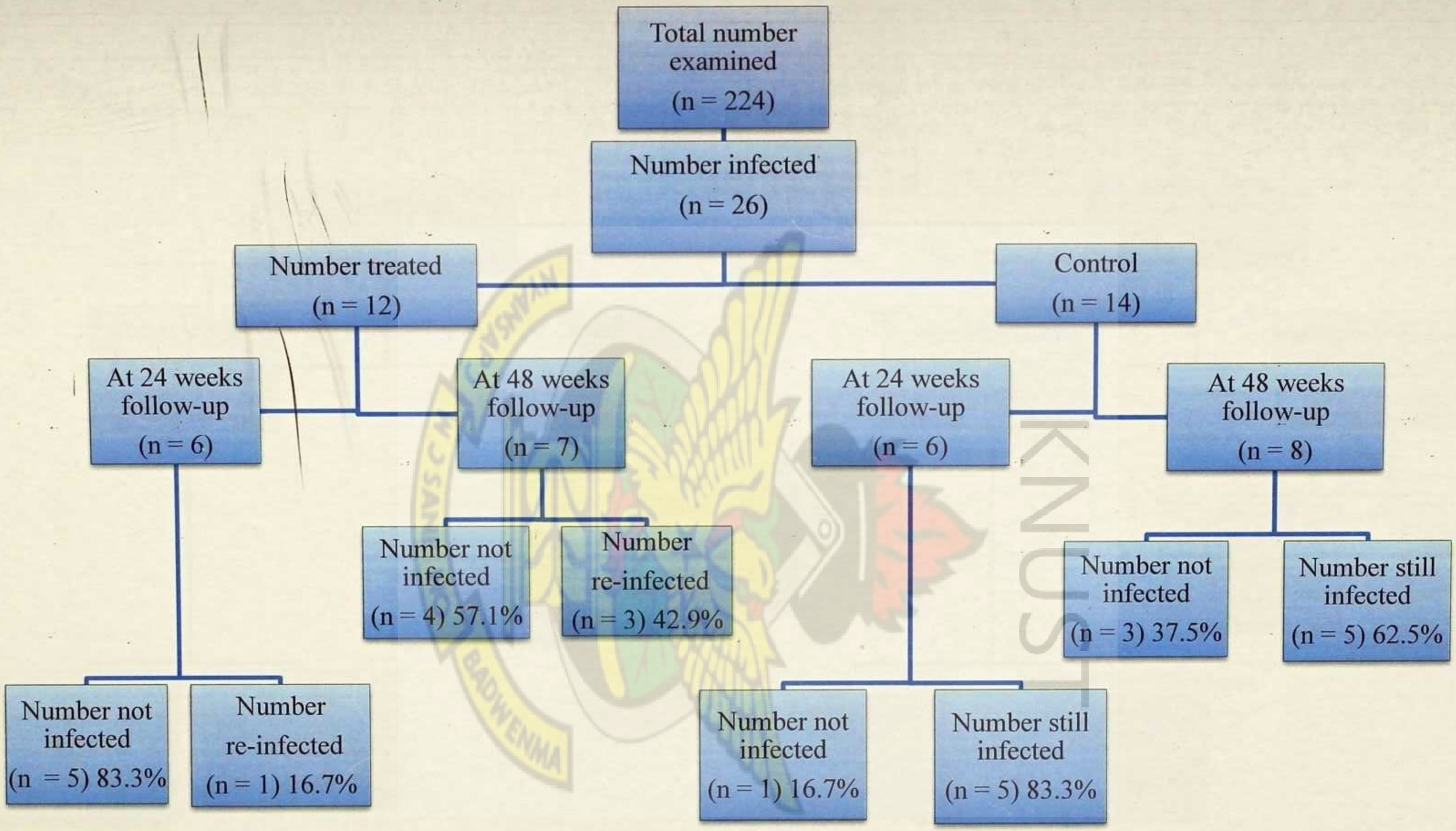

Figure 4.3 Participant flow chart for *schistosoma haematobium* infections

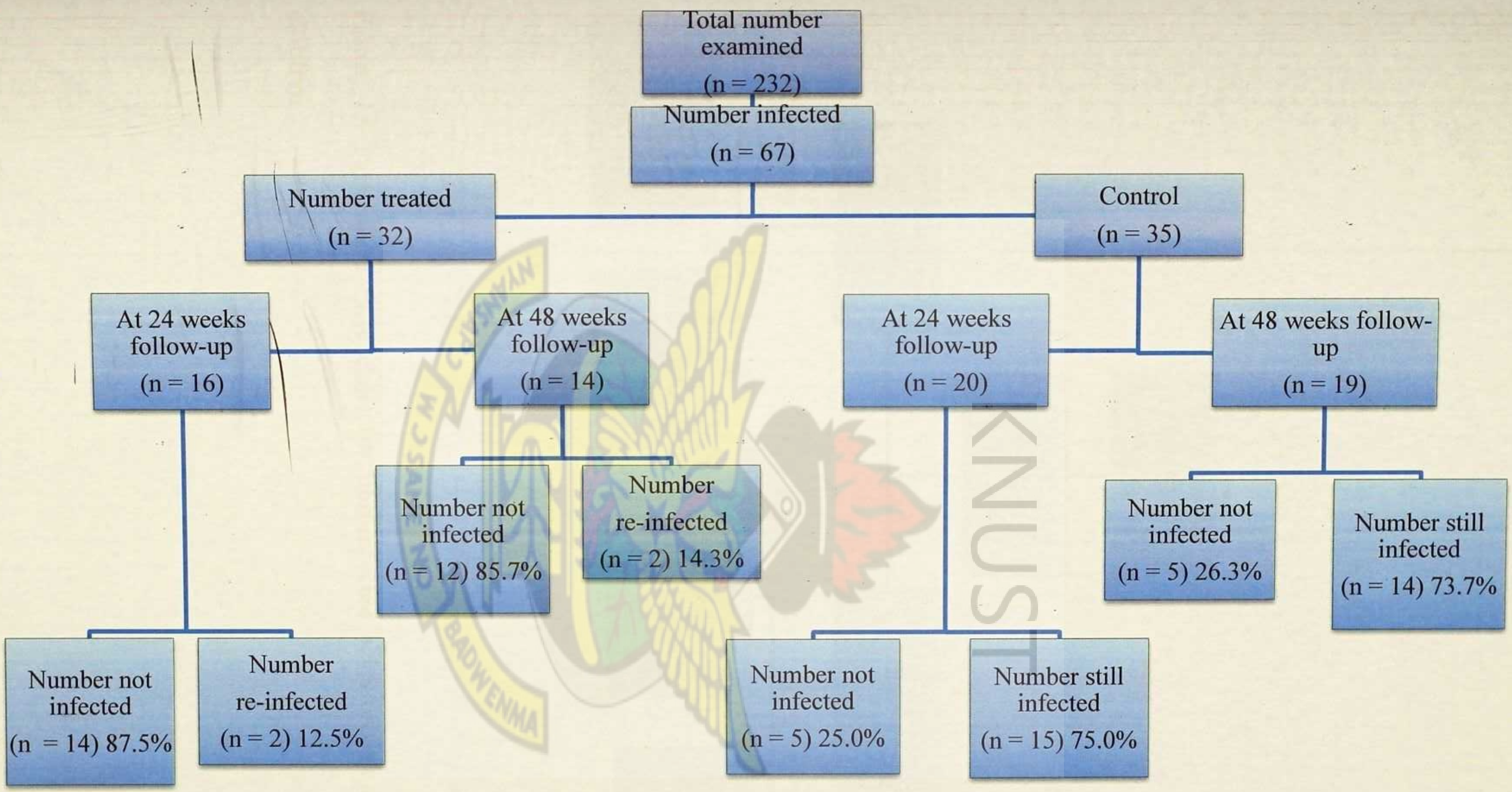

Figure 4.4 Participant flow chart for *schistosoma mansoni* infections

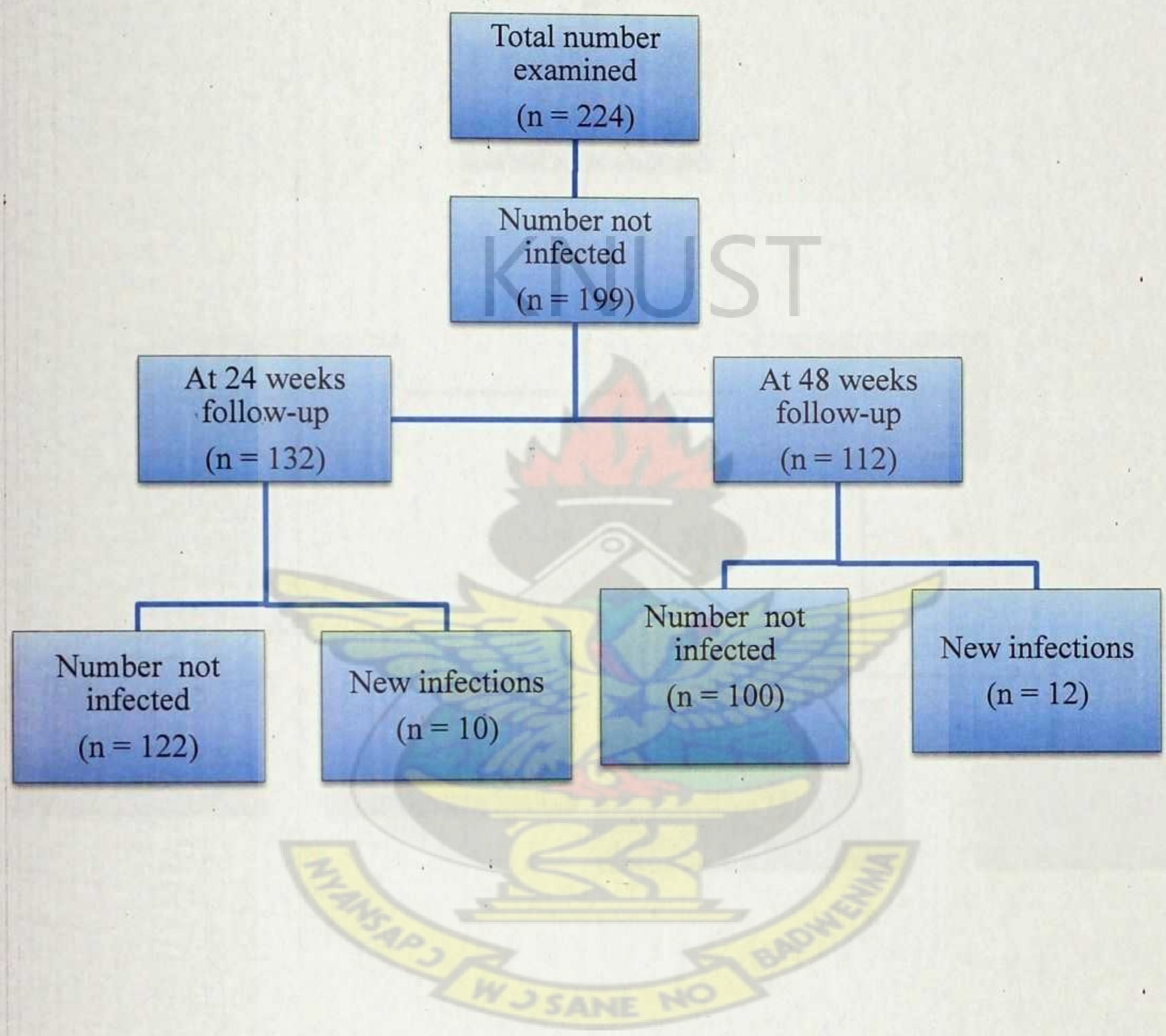

Figure 4.5 Participant flow chart for non-infected *schistosoma haematobium* children

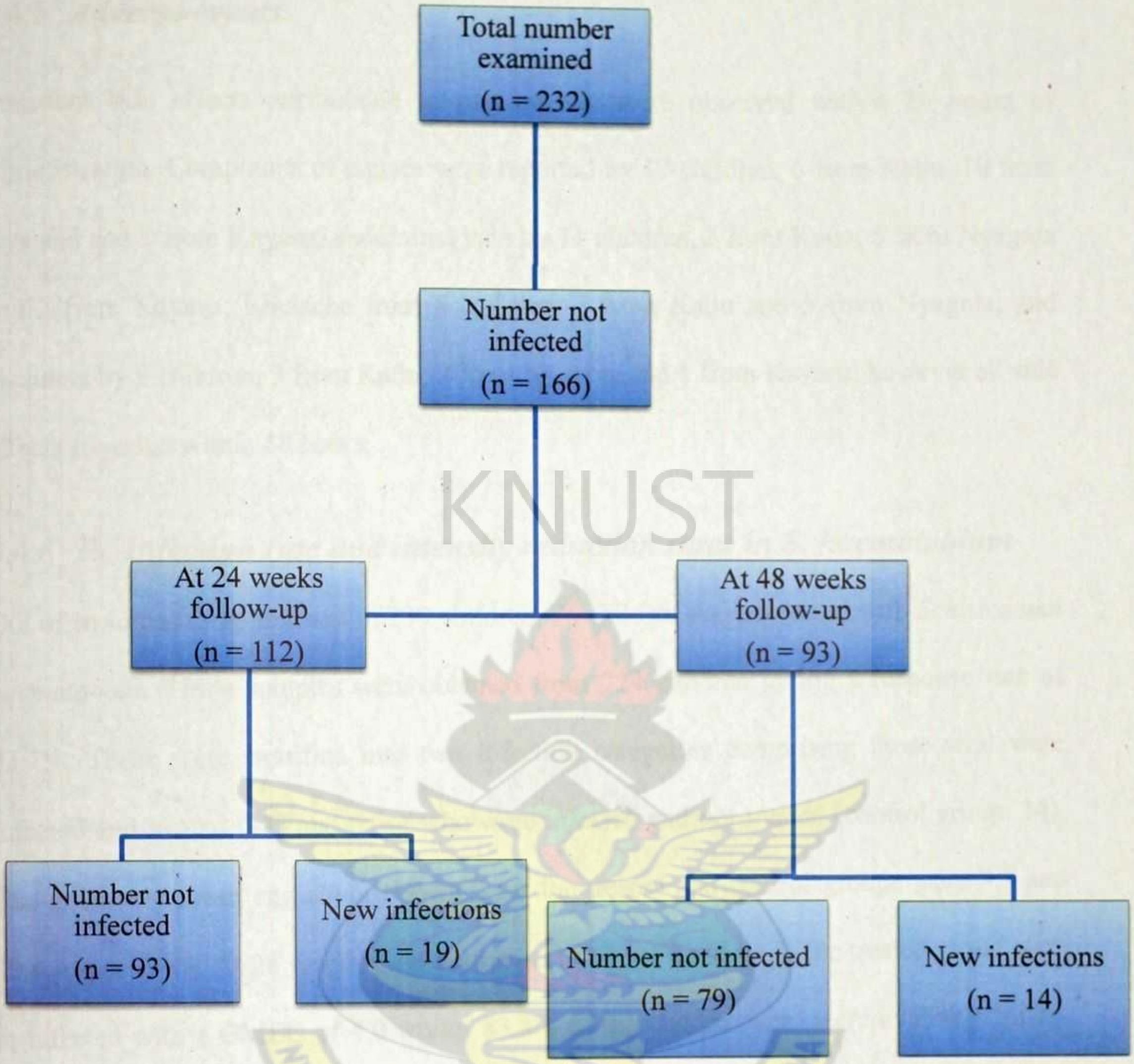

Figure 4.6 Participant flow chart for non-infected *schistosoma mansoni* children

4.4.5 *Adverse events*

Transient side effects attributable to praziquantel were observed within 24 hours of administration. Complaints of nausea were reported by 17 children, 6 from Katiu, 10 from Nyagnia and 1 from Kayoro; abdominal pain by 11 children, 3 from Katiu, 6 from Nyagnia and 2 from Kayoro; headache from 8 children, 3 from Katiu and 5 from Nyagnia; and dizziness by 6 children, 3 from Katiu, 2 from Nyagnia and 1 from Kayoro; however all side effects subsided within 48 hours.

4.4.6 *Re-infection rate and intensity reduction rates in S. haematobium*

Out of an initial sampling size of 239 children, 26 children were infected with *Schistosoma haematobium*. Urine samples were obtained from 224 children giving a response rate of 93.7%. These were stratified into two infection categories comprising those who were infected and treated (11) and those who were infected and not treated (control group, 14).

The geometric mean egg count (GMEC) for the treated and control groups were 9.7 and 10.4 respectively. At 24 weeks post-treatment, 16.7% of children in the treated group were re-infected with a GMEC of 4.0 whiles 83.3% of the children who were available for re-examination in the control group were still infected with a GMEC of 30.3. At 48 weeks post-treatment, 42.9% of the children who were in the treated group were re-infected with a GMEC of 2.0 whiles 62.5% of the children who were available for re-examination in the control group were still infected with a GMEC of 25.2. Intensity reduction rates of 58.8% and 79.4% were recorded for children in the treated group at 24 and 48 weeks post-treatment respectively. However, in the control group negative intensity reduction rates were recorded at 24 and 48 weeks post-treatment (-191.3% and -142.3% respectively).

rates of 83.3% (5/6) and 50.0% (4/8) were recorded for children in the treatment group at 24 and 48 weeks post-treatment respectively. Of the 199 children who were not infected at the initial sampling, 122(61.3) remained not infected and 10(5.0%) new infections were recorded at 24 weeks whiles 100(50.3) remained not infected and 12(6.0%) new infections were recorded at 48 weeks (Table 4.3).

Table 4.3 Re-infection rates, geometric mean egg counts and intensity reduction rates in study participants infected with *S. haematobium* at 24 weeks and 48 weeks after treatment with praziquantel.

STUDY PERIODS	STUDY GROUPS		
	TREATED	CONTROL	TOTAL
Before Treatment			
Number of children infected	11/25	14/25	25
GMEC	9.7	10.4	10.1
Follow-up			
24 weeks			
Number Infected	1/6	5/6	11
Re-Infection Rate (%)	16.7	-	-
GMEC	4.0	30.3	21.6
Intensity Reduction Rate (%)	58.8	-191.3	-113.9
48 weeks			
Number Infected	3/7	5/8	15
Re-Infection Rate (%)	42.9	-	-
GMEC	2.0	25.2	9.7
Intensity Reduction Rate (%)	79.4	-142.3	4.0

GMEC = Geometric mean egg count per 10 mL of urine (antilog of the mean of all log transformed egg counts + 1); Intensity reduction rate = [1 – (GM egg counts per 10 mL of urine after treatment/GM egg counts per 10 mL before treatment)] X 100; Re-Infection Rate = [No. infected in treated group / No. Treated and present at follow-up] X 100.

4.4.7 *Re-infection rate and intensity reduction rates in S. mansoni*

Out of the 239 children examined, 67 were infected with *schistosoma mansoni*. Stool samples were obtained from 232 children giving a response rate of 97.1%. These were stratified into two infection categories comprising those who were infected and treated (31) and those who were infected and not treated (control group, 35). The geometric mean egg counts (GMEC) for the treated and control groups were 130.1 and 182.0 respectively. At 24 weeks post-treatment, 2 out of 16 children (Table 4.4) in the treated group were re-infected with a GMEC of 80 whiles 15 of the 20 children in the control group were still infected with a GMEC of 212. At 48 weeks post-treatment, 2 out of 14 children (Table 4.4) in the treated group were re-infected with a GMEC of 226.3 whiles 14 out of 19 children in the control group were still infected with a GMEC of 189. A positive intensity reduction rate of 38.5% was observed for children in the treated group at 24 weeks while at 48 weeks a poor intensity reduction rate (-73.9%) was observed. However, in the control group, intensity reduction rates of -16.5% and -3.8% were observed at 24 and 48 weeks post-treatment respectively. Cure rates of 82.4% (14/17) and 75% (12/16) were estimated for children in the treatment group at 24 and 48 weeks post-treatment respectively. Of the 166 children who were not infected at the initial sampling, 93 were still not infected at 24 weeks and 79 at 48 weeks. New infections of 19(11.4%) and 14(8.4%) were estimated at 24 weeks and 48 weeks respectively.

Table 4.4 Re-Infection Rates, geometric mean egg counts and intensity reduction rates in study participants infected with *S. mansoni* at 24 weeks and 48 weeks after treatment with praziquantel.

STUDY PERIODS	STUDY GROUPS		
	TREATED	CONTROL	TOTAL
Before treatment			
Number of children infected	31/67	35/67	67
GMEC	130.1	182.0	155.5
Follow-up			
24 weeks			
Number Infected	2/16	15/20	36
Re-Infection Rate (%)	12.5	-	-
GMEC	80	212	189.1
Intensity Reduction (%)	38.5	-16.5	-21.6
48 weeks			
Number Infected	2/14	14/19	35
Re-Infection Rate (%)	14.3	-	-
GMEC	226.3	189	193.3
Intensity Reduction (%)	-73.9	-3.8	-24.3

GM = Geometric mean egg count per g of stool (antilog of the mean of all log transformed egg counts + 1); Intensity reduction rate = [1 – (GM egg counts per g of stool after treatment/GM egg counts per g of stool before treatment)] X 100; Re-Infection rate = [No. infected in treated group / No. Treated and present at follow-up] X 100.

4.5 ANALYZED RESPONSES TO QUESTIONNAIRE

From Table 4.5, analysis of responses to the questionnaire for *S. haematobium* and *S. mansoni* infections showed 98.2% (108/110) of the subjects from Nyagnia having more contact with water bodies compared to 71.6% (68/95) ($p < 0.0001$) and 88.2% (30/34) ($p = 0.0112$) of the subjects from Katiu and Kayoro respectively. There was a marginal significance of subjects in Kayoro having contact with water bodies when compared to subjects from Katiu ($p = 0.0511$). More subjects from Katiu (97.7%; 93/95) engaged mostly in crop and fish farming activities compared to 90% (99/110) from Nyagnia ($p = 0.0207$) whilst a comparison of subjects from Kayoro (100%; 34/34) and Katiu showed subjects from Kayoro engaging more in farming activities ($p = 0.055$). On analyzing some signs and symptoms associated with *S. haematobium* and *S. mansoni* infections, a significantly higher number of subjects in Katiu (70.5%; 67/95) reported of body weakness compared to 40.9% (45/110) ($p < 0.0001$) and 50.0% (17/34) in Nyagnia and Kayoro respectively. The same trend was observed in subjects with bloody stool, with 53.7% (51/95) subjects from Katiu compared to 28.2% (31/110) and 14.7% (5/34) in Nyagnia and Kayoro respectively. No significant differences were observed in the proportion of subjects with bloody urine from the three study sites ($p > 0.05$).

Table 4.5 Analysis of responses to questions on predisposing factors and signs & symptoms associated with *S. mansoni* and *S. haematobium* infections

Variable	STUDY SITE					
	Katiu (n=95)	Nyagnia (n=110)	Kayoro (n=34)	p^a	p^b	p^c
Have contact with water bodies	68(71.6)	108(98.2)	30(88.2)	<0.0001	0.0511	0.0112
Engage in fish & crop farming	93(97.7)	99(90.0)	34(100.0)	0.0207	0.3938	0.0550
Body weakness	67(70.5)	45(40.9)	17(50.0)	<0.0001	0.0312	0.3494
Bloody urine	28(29.5)	43(39.1)	16(47.1)	0.1490	0.0634	0.4090
Bloody stool	51(53.7)	31(28.2)	5(14.7)	0.0002	<0.0001	0.1127

Data are presented as proportions. p^a defines the level of significance when Katiu was compared to Nyagnia; p^b defines the level of significance when Katiu was compared to Kayoro; p^c defines the level of significance when Nyagnia was compared to Kayoro

4.6 RISK VARIABLES FOR *S. HAEMATOBIUM* AND *S. MANSONI* INFECTION

Table 4.6 shows univariate analysis of some risk variables and signs & symptoms associated with *S. haematobium* and *S. mansoni* infections. Subjects who were males were 3.4 times at risk of being infected with *S. haematobium* infection (p = 0.018), while subjects who were involved in farm work had a less likelihood of being infected with *S. haematobium* (cOR = 0.2) (p = 0.011). Subjects who reported positively to having blood in

their urine were 3.0 times at risk of being infected with *S. haematobium* (p = 0.012). Males were 5.0 times at risk of being infected with *S. mansoni* (p = <0.0001) with subjects who had contact with water bodies having 4.5 times likelihood of being infected with *S. mansoni* (p = 0.016). Subjects who were involved in farm work had a less likelihood of being infected with *S. mansoni* (cOR = 0.2) (p = 0.027). However, subjects who reported of ever being treated for schistosomiasis were 2.5 times at risk of being infected with *S. mansoni* (p = 0.014).

Table 4.6 Univariate analysis of risk variables and signs & symptoms associated with *S. haematobium* and *S. mansoni* infections

	S. haematobium infection			*S. mansoni infection*		
Variable	cOR	95% CI	p-value	cOR	95% CI	p-value
Age	0.9	0.8 - 1.1	0.433	0.9	0.8 - 1.0	0.124
Sex (male*)	3.4	1.2 - 9.4	0.018	5.0	2.5 - 10.0	<0.0001
Weight	1.0	0.9 - 1.0	0.347	1.0	0.9 - 1.0	0.051
Contact with water bodies	2.0	0.4 - 8.9	0.362	4.5	1.3 - 15.2	0.016
Farm work	0.2	0.1 - 0.7	0.011	0.2	0.1 - 0.9	0.027
Weakness	0.6	0.3 - 1.5	0.292	1.0	0.5 - 2.0	0.992
Bloody urine	3.0	1.3 - 6.9	0.012	NA	NA	NA
Bloody stool	NA	NA	NA	1.3	0.7 - 2.3	0.423
Schistosomiasis history	1.2	0.4 - 3.5	0.754	1.2	0.6 - 2.4	0.615
Ever treated	1.3	0.4 - 4.2	0.652	2.5	1.2 - 5.3	0.014

*cOR = crude odds ratio; CI = confidence interval; * = response variable; NA = not applicable*

Table 4.7 shows a sex adjusted multivariate analysis for risk variables and signs and symptoms associated with *S. haematobium* and *S. mansoni* infections. Upon adjusting for sex, subjects who were engaged in farm work remained less likely of being infected with *S. haematobium* (cOR = 0.2) (p = 0.040) while subjects who reported of bloody urine were still at risk of being infected with *S. haematobium* (cOR = 2.5) (p = 0.037).

For *S. mansoni* infections, sex adjustment resulted in age being a protective factor for infection (cOR = 0.9) (p = 0.038). Subjects who had ever been treated for *S. mansoni* infection had a 2.4 times likelihood of being infected (p = 0.031).

Table 4.7 Sex adjusted odds ratio for risk variables and signs and symptoms associated with *S. haematobium* and *S. mansoni* infections

Variable	*S. haematobium*			*S. mansoni*		
	*adj*OR	95% CI	p value	*adj*OR	95% CI	p value
Age	0.9	0.8 - 1.1	0.298	0.9	0.8 - 1.0	0.038
Weight	1.0	0.9 - 1.0	0.371	1.0	0.9 - 1.0	0.060
Contact with water bodies	1.4	0.3 - 6.3	0.698	2.9	0.8 - 10.4	0.097
Farm work	0.2	0.1 - 0.9	0.040	0.3	0.1 - 1.3	0.120
Weakness	0.7	0.3 - 1.8	0.522	1.4	0.7 - 2.8	0.355
Bloody urine	2.5	1.1 - 6.0	0.037	-	-	-
Bloody stool	-	-	-	1.4	0.7 - 2.5	0.331
Schistosomiasis history	1.2	0.4 - 3.7	0.709	1.3	0.6 - 2.7	0.505
Ever treated	1.2	0.4 - 3.8	0.785	2.4	1.1 - 5.3	0.031

adjOR = adjusted odds ratio

Chapter 5

DISCUSSION

Schistosomiasis remains a public health problem and plans by the World Health Organization and the Ministry of Health of Ghana to embark on a mass drug administration in endemic areas make it imperative for an evaluation of the efficacy of the standard single dose of praziquantel.

In this study, the epidemiology of schistosomiasis and the effectiveness of praziquantel which is the drug of choice for treatment of *S. haematobium* and *S. mansoni* are assessed before and after treatment, among primary school children in the Kassena/Nankana west district. This study serves to ascertain the prevalence rate and intensity of schistosomiasis, the efficacy of the standard single dose of 40 mg/kg body weight praziquantel in a mass drug administration and the re-infection rates of *S. haematobium* and *S. mansoni* after treatment.

5.1 PREVALENCE OF SCHISTOSOMA HAEMATOBIUM AND SCHISTOSOMA MANSONI INFECTION

In a two-year (2007 – 2008) strategic plan for integrated neglected tropical disease control in Ghana by the Ministry of Health/Ghana Health Service, it was reported that urinary schistosomiasis caused by *S. haematobium* is widespread in all parts of the country and intestinal schistosomiasis caused by *S. mansoni* is restricted and patchy in its distribution while available data to determine the extent and severity of the national level of schistosomiasis dates back to the 1970s. The results of this study indicated *S. haematobium* and *S. mansoni* infection prevalence rates of 10.9% and 28.0% respectively suggesting that both infections are currently prevalent in the Kassena/Nankana West District of the Upper-

East Region. Different prevalence rates of schistosomiasis have been quoted in Ghana with Aboagye and Edoh (2009) reporting a 52% *S. haematobium* prevalence rate in Mahem and Galilea communities in Accra, 34.4% in Cape Coast (Okanla *et al.*, 2003) and 90% among children in some communities along the Volta lake (Paperna, 1969) when it was created.

The different species of intermediate hosts (*Bulinus globosus* for *S. haematobium* and *Biomphalaria pfeifferi* for *S. mansoni*) adapt best to varying environmental conditions which support their survival, thus, though both *S. haematobium* and *S. mansoni* infections have been reported as being prevalent in the Kassena/Nankana West District (Amankwah *et al.*, 1994), it was observed that the infection prevalence of each species in each study site was unique with predominantly *S. mansoni* infections in Katiu, mixed (both *S. haematobium* and *S. mansoni*) infections in Nyagnia and *S. haematobium* infections in Kayoro. The variation in schistosomiasis prevalence in the three study sites within the Kassena/Nankana West District could therefore be related to the highly dispersed nature of the study sites, thus contact of inhabitants solely with water bodies in their localities which harbour specific intermediate hosts. The above prevalence supports the report of high transmission of schistosome species in areas close to the Tono irrigation scheme in an earlier study in the Kassena/Nankana Districts by Amankwah *et al* (1994) which showed that both schistosome species were highly transmitted among school children in areas close to the Tono irrigation scheme with that of *S. haematobium* taking place in all parts of the irrigation system (lateral canal, night storage dam and main reservoir) while that of *S. mansoni* takes place only in the main canal. The Tono irrigation scheme does not extend to Katiu and Kayoro thus inhabitants of these two study sites rely on dams in their locality as a source of water. Nyagnia is however situated in close proximity to the Tono irrigation

scheme and analysis of some predisposing factors for schistosome infections showed that among the three study sites, children from Nyagnia are more likely to have contact with water bodies compared to their counterparts from Katiu ($p = <0.0001$) and Kayoro ($p = 0.0112$) and to be infected with both schistosome species (mixed infections) ($p = 0.0003$).

5.2 PREVALENCE OF *SCHISTOSOMA HAEMATOBIUM* BY PREDISPOSING FACTORS, SIGNS AND SYMPTOM

This study showed that, being a male was significantly associated with a 3.4 times risk of being infected with *S. haematobium* whilst a three (3) times risk was associated with reporting of bloody urine. Engagement in farming activities was associated with a less likelihood of being infected. The high relative risk (cOR = 3.4) associated with *S. haematobium* infection among males in this study is in agreement with the findings of Nsowah-Nuamah et al., (2001) who nonetheless reported a lower risk of 1.8 times. This finding from the present study can be attributed to male children having more contact with water bodies in the districts compared to their female counterparts and further reflects a general lack of behavioural change and educational talks on preventive measures for *S. haematobium* infection in the district. Aboagye and Edoh., (2009) however reported that both sexes were equally vulnerable, and attributed it to both sexes having equal contact with infested water, thus, expressing a multifactorial nature of urinary schistosomiasis. Children within the age group of 11 – 15 years in this study had the highest prevalence of infection. This finding is in agreement with reports by Nkegbe (2010) and Nsowah-Nuamah *et al* (2001); reasons which can be attributed to the high affinity of these groups of children for water, especially contact of the type that is most likely to lead to infection, such as

swimming, fetching water, playing in the water among others which have been identified to be risk factors in earlier studies (Jeans and Schwellnus, 1994; Useh and Ejezie, 1999).

It has been estimated that *S. haematobium* causes haematuria (bloody urine) in about 70 million individuals in sub-Saharan Africa (van der Werf *et al.*, 2003), with Aboagye and Edoh (2009) in a study of risk factors associated with urinary schistosomiasis reporting a 4.5 times relative risk for haematuria in infected children. The corresponding high odds ratio (OR) associated with haematuria for *S. haematobium* infection in this study agrees with finding by Aboagye and Edoh (2009), reiterating haematuria as a presumptive diagnostic sign for *S. haematobium* infection.

5.3 PREVALENCE OF *SCHISTOSOMA MANSONI* BY PREDISPOSING FACTORS, SIGNS AND SYMPTOMS

Univariate logistic regression analysis of associated risk factors and signs and symptoms for *S. mansoni* obtained in this study showed that being a male, having water contact and having ever been treated for schistosomiasis were significantly associated with *S. mansoni* infection. Such significant findings from the above mentioned risk variables point to the fact that, children in the Kassena/Nankana West District are at a higher risk of being infected with *S. mansoni.* The crude odds ratios estimated for the risk variables from this study were sex (5.0), having contact with water bodies (4.5) and being ever treated (2.5) and are in agreement but relatively higher in relation to that of El-Khoby *et al.,* (2000) in Egypt which were sex (1.6), having contact with water bodies (2.3) and being ever treated (1.5). Upon adjusting for sex, the 2.4 times relative risk associated with ever being treated for *S. mansoni* after prior treatment buttresses the point that children who have ever been treated develop existing habits which keep them in continuous contact with infested water

bodies. The above observation reiterates the general lack of attitudinal change, lack of educational preventive processes and lack of scheduled treatment regimen for children in such high risk zones. The relatively less risk of being infected with *S. mansoni* as one ages (15+ age group) after adjusting for sex in this study could be attributed to reduced exposure to cercaria infested water. This is because advancement in age is associated with less engagement in high risk exposure activities such as swimming, washing, bathing at water source and walking barefooted among others. There is also a possibility that adults might have developed an acquired immunity to schistosome infection in previous infections as well as a slow spontaneous death of adult worms from early infections (Butterworth, 1998).

A WHO report (1993) outlined the type of irrigation, operation and maintenance of irrigation schemes and the selection of crops as important aspects of irrigation that determine schistosomiasis epidemiology. From this study, farm work was associated with a reduced risk for both infections (*S. haematobium and S. mansoni*) in the univariate analysis and remained a less significant risk factor for *S. haematobium* infection upon adjusting for sex in a multivariate analysis. Farming is the main source of income and livelihood for families in the Kassena/Nankana District with most parents going about their daily chores virtually barefooted and with little protective gear in the form of gloves and boots (personal *observation*). This habit of not wearing protective gear during farm work is expected to have caught on with the children, however, the absence of a significant finding in the risk for both *S. haematobium* and *S. mansoni* infections in both univariate and sex adjusted analysis does not support the above expectation and thus cannot be extrapolated from the remits of this study and as such will require further investigations.

5.4 TREATMENT OF SCHISTOSOMIASIS WITH PRAZIQUANTEL

5.4.1 *Parasitological Re-Infection Rates and Intensity Reduction*

5.4.1.1 *Schistosoma haematobium*

Declarations of a high efficacy of the standard dose of 40 mg/kg body weight praziquantel (WHO, 1985) provide expectation for high intensity reduction rate especially in children in highly endemic areas. At 24 and 48 weeks post-treatment, this study reported re-infection rates of 16.7% and 42.9% respectively. The re-infection rate observed at 24 weeks (6 months) was lower compared to that observed at 48 weeks. The high re-infection rate observed after treatment could be due to high transmission levels in these areas characterized by behavioural factors such as bathing, washing clothes, fishing and swimming in cercaria infested water; especially in the <15 years age group due to their frequent contact with water. This finding was imminent in the high percentage of children who had contact with water bodies in the communities and number of new infections detected at follow-ups. The lack of acquired immunity in children of this age group to schistosomiasis infection could also be a possible reason for the high risk of re-infections as suggested in earlier studies on immune response and re-infection (Hagan *et al.*, 1987; Etard *et al.*, 1995).

Significant reductions in geometric mean egg counts (GMEC) were observed in the treated children at 24 and 48 weeks follow-up time points which translated into increased intensity reduction rates. This observation was however contrary to the control group where GMECs at 24 and 48 weeks follow-ups went up by 191.3% and 142.3% respectively, resulting in negative intensity reduction rate estimations. The reduction in egg counts in treated *S. haematobium* infected children is evident of the fact that a single dose of praziquantel has

the efficacy to reduce worm load and egg counts for as long as 48 weeks notwithstanding the high re-infection rates associated with high transmission levels.

5.4.1.2*Schistosoma mansoni*

Re-infection rates of 12.5% and 14.3% were observed at 24 and 48 weeks respectively in this study. Compared to counts at the initial sampling stage, the lower re-infection rate observed at 24 weeks follow-up time point and reductions in GMEC within this period could be associated with the efficacy of treatment. The increase in GMEC at 48 weeks follow-up time point beyond that observed at the initial sampling stage resulted in a negative intensity reduction rate at 48 weeks, indicating a high transmission rate which translated to higher re-infection rates. An intensity reduction rate of 95% is recommended one year after treatment with praziquantel for *S. mansoni* infections in those not completely cured. Intensity reduction rates estimated from this study were at variance with WHO (1985) recommendations, thus, giving an indication of praziquantel not being able to fully reduce the intensity of *S. mansoni* worm loads and egg counts one year after treatment.

This finding, nevertheless, cannot be interpreted as evidence for praziquantel resistance given reasons such as single round of therapy, annual re-infection rates, and reports of resistance of immature forms to the standard dose of praziquantel as related in the study of Xiao *et al.*, (1985). Given the credence for high transmission levels, intra-specimen or inter-specimen variations of egg excretion and inherent limitations of the Kato-Katz technique such as its lack of sensitivity (Engels *et al.*, 1996; Utzinger *et al.*, 2001) could be possible reasons contributing to the finding of a high number of newly infected children, who, in reality, might have had actual infections that may have been missed. Although lower re-infection rates were observed for *S. mansoni* infection as compared to *S.*

haematobium infections after treatment with a single dose of 40 mg/kg body weight praziquantel, gg counts contrarily remained elevated among the children within the control group.

Chapter 6

CONCLUSION

In conclusion, this study showed that the Kassena/Nankana District is endemic for both *S. haematobium* and *S. mansoni* infections. The infection is prevalent among 6 - 17 years old children of school going age; (peaks at 11 – 15 years) and the rate of transmission and re-infection after treatment with a dose of 40 mg/kg praziquantel within a year is quite high. It suffices to say that annual administration of a single dose of praziquantel does not afford total protection to the children in the district from both schistosome species all year round.

6.1 LIMITATIONS OF THE STUDY

1. It is accepted that the Kato-Katz technique is not too sensitive. Over the years several adaptations of the Kato-Katz technique have been proposed, indicating a lack of consensus on an ideal technique. Since its introduction, egg count is known to be subjected to important variability and the Kato-Katz technique, the current standard method for the field diagnosis of intestinal schistosomiasis, is not an exception.

The limitations of the Kato-Katz technique include the following

- The calculation of eggs per gram is based on the assumption that the density of a stool sample is equal to 1.0, as templates determine a defined volume, not a weight. Hence, any change in the consistency of stools will influence the results.
- The method lacks sensitivity for the detection of light infections.
- The use of a single stool sample can severely underestimate true *S. mansoni* prevalence. This could be as a result of the inter-specimen (day-to-day) and intra-specimen (within the same stool) variations of egg count in individuals partly due to the low concentrations and uneven distribution of eggs in stools.

2. The major limitation for the urine filtration technique is the high cost associated with membrane filter and holder acquisition.

6.2 RECOMMENDATION

Because of the morbidity borne by children of school going age and their role as reservoirs for community infections, serious measures should be taken to control the disease in the district by

1. Administering a single dose of 40mg/kg praziquantel biannually with six months intervals will be beneficial to children in the district.
2. Implementation of control and preventive measures against schistosomiasis.
3. Collecting more than one sample (especially stool) for examinations from each participant in subsequent studies will help overcome the inherent limitations of the Kato-Katz thick smear method.
4. Further research into schistosome infections should be conducted among children who do not attend school in the Kassena/Nankana West District to assess their prevalence and risks associated with schistosomiasis in order to ascertain the variations.
5. Considering the paucity of data on *S. mansoni* prevalence rates in the country and the relatively high prevalence rate estimated from this study, resources and interest should be devoted to *S. mansoni* prevalence research in future studies.

REFERENCES

Aboagye I.F. and Edoh D. (2009) Investigation of the risk of infection of urinary schistosomiasis at Mahem and Galilea communities in the Greater Accra region of Ghana. *West African Journal of Applied Ecology* 15.

Amankwah J.A., Bloch P., Meyer-Lassen J., Olsen A. and Christensen N.O. (1994) Urinary and intestinal schistosomiasis in the Tono irrigation Scheme, Kassena/Nankana district, Upper east region, Ghana. *Trop Med Parasitol.* 45, 319-323.

Amer M. (1982) Cutaneous schistosomiasis. *Int J Dermatol* 21, 44-46.

Ampofo J.A. and Zuta P.C. (1996) Schistosomiasis in the Weija Lake: A case study on the public health importance of man-made lakes. 1, 191-195.

Andrade Z.A. (1964) Warren Ks: Mild Prolonged Schistosomiasis in Mice: Alterations in Host Response with Time and the Development of Portal Fibrosis. *Trans R Soc Trop Med Hyg* 58, 53-57.

Andrews P. (1981) A summary of the efficacy of praziquantel against schistosomes in animal experiments and notes on its mode of action. *Arzneimittelforschung* 31, 538-541.

Andrews P. (1985) Praziquantel: mechanisms of anti-schistosomal activity. *Pharmacol Ther* 29, 129-156.

Arinola O.G. (2005) Immunological aspects of urinary schistosomiasis in Ibadan, Southwestern Nigeria. *Annals of Ibadan Postgraduate Medicine* 3, 69-73.

Badr M.M. (1986) *Surgical management of urinary Bilharziasis*. London.

Barlow C.H. (1936) Is there dermatitis in Egyptian schistosomiasis? *Am. J. Hyg.* 24, 587-599.

Barsoum R.S. (1992) The Egyptian transplant experience. *Transplant Proc* 24, 2417-2420.

Barsoum R.S. (1993) Schistosomal glomerulopathies. *Kidney Int* 44, 1-12.

Bassily S., Farid Z., Barsoum R.S., Soliman L.A., Higashi G.I. and Miner W.F. (1976) Renal biopsy in Schistosoma-Salmonella associated nephrotic syndrome. *J Trop Med Hyg* 79, 256-258.

Bergquist N.R. (1998) Schistosomiasis vaccine development: progress and prospects. *Mem Inst Oswaldo Cruz* 93 Suppl 1, 95-101.

Bilharz T. (1852) A study of human helminthography with brief observations by Bilharz in Cairo along with remarks by Siebald. *Breslau Z Wissensch Zool* 4, 53-72.

Bina J.C., Tavares-Neto J., Prata A. and Azevedo E.S. (1978) Greater resistance to development of severe schistosomiasis in Brazilian Negroes. *Hum Biol* 50, 41-49.

Bonnard P., Remoue F., Schacht A.M., Deuffic-Burban S., Dompnier J.P., Elguero E., Charrier N., Cassagnou M., Diop M., Ly A., Capron A. and Riveau G. (2004) Specific isotype immune response in the diagnosis of human schistosomiasis pathology? *Am J Trop Med Hyg* 71, 202-205.

Boros D.L. (1987) *Granuloma and fibrosis*. Suresnes: Fondation Franco-Allemande.

Boros D.L. (1989) Immunopathology of Schistosoma mansoni infection. *Clin Microbiol Rev* 2, 250-269.

Boros D.L., Pelley R.P. and Warren K.S. (1975) Spontaneous modulation of granulomatous hypersensitivity in schistosomiasis mansoni. *J Immunol* 114, 1437-1441.

Boyd R.F. (1995) *Basic medical microbiology*, Fifth ed. Boston: Little, Brown and company.

Brack M., McPhaul J.J., Damian R.T. and Kalter S.S. (1972) Glomerular lesions in "normal" and schistosoma mansoni-infected baboons *(papio cynocephalus)*. *J Med Primatol* 1, 363-373.

Brindley P.J. (1994) Drug resistance to schistosomicides and other anthelmintics of medical significance. *Acta Trop* 56, 213-231.

Brindley P.J. and Sher A. (1990) Immunological involvement in the efficacy of praziquantel. *Exp Parasitol* 71, 245-248.

Brito E., Santoro F., Rocha H., Dutra M. and Capron A. (1979) Immune complexes in schistosomiasis. VI--Circulating IC levels in patients with and without nephropathy. *Rev Inst Med Trop Sao Paulo* 21, 119-124.

Butterworth A.E. (1998) Immunological aspects of human schistosomiasis. *Br Med Bull* 54, 357-368.

Capron A., Yokogawa M., Biguet J., Tsuji M. and Luffau G. (1965) [Immunologic diagnosis of human paragonimosis. Demonstration of specific serum antibodies by immunoelectrophoresis]. *Bull Soc Pathol Exot Filiales* 58, 474-487.

Carlier Y., Bout D., Bina J.C., Camus D., Figueiredo J.F. and Capron A. (1975) Immunological studies in human schistosomiasis. I. Parasitic antigen in urine. *Am J Trop Med Hyg* 24, 949-954.

Carlier Y., Bout D. and Capron A. (1980) Detection of Schistosoma mansoni M antigen in circulating immune-complexes and in kidneys of infected hamsters. *Trans R Soc Trop Med Hyg* 74, 534-538.

Cheesbrough M. (1999) *District Laboratory Practice in Tropical countries 1*. Cambridge: Cambridge University Press.

Cheever A.W., Duvall R.H. and Hallack T.A., Jr. (1983) Hepatic fibrosis in Schistosoma haematobium-infected mice. *Trans R Soc Trop Med Hyg* 77, 673-679.

Cheever A.W., Torky A.H. and Shirbiney M. (1975) The relation of worm burden to passage of Schistosoma haematobium eggs in the urine of infected patients. *Am J Trop Med Hyg* 24, 284-288.

Chen M.G. and Mott K.E. (1989) Progress in assessment of morbidity due to schistosomiasis. Reviews of recent literature: Schistosoma haematobium, schistosoma intercalatum, schistosoma japonicum, schistosoma mansoni. London: Bureau of Hygiene and Tropical Diseases.

Damian R.T. (1984) Immunity in schistosomiasis: a holistic view. *Contemp Top Immunobiol* 12, 359-420.

Davies S.J. and McKerrow J.H. (2001) *Biology of parasitism*. Boston.

Davis A. (1993) *Antischistosomal drugs and clinical practice*. Wallingford: CAB International.

Davis A. and Wegner D.H. (1979) Multicentre trials of praziquantel in human schistosomiasis: design and techniques. *Bull World Health Organ* 57, 767-771.

De Brito T., Gunji J., Caravolo A. and Da Silva L.C. (1971) Glomerular lesions in experimental infections of Schistosoma mansoni in Cebus apella monkeys. In *Bull WHO*, pp. 419-422.

De Cock K.M. (1986) Hepatosplenic schistosomiasis: a clinical review. *Gut* 27, 734-745.

de Jesus A.R., Silva A., Santana L.B., Magalhaes A., de Jesus A.A., de Almeida R.P., Rego M.A., Burattini M.N., Pearce E.J. and Carvalho E.M. (2002) Clinical and immunologic evaluation of 31 patients with acute schistosomiasis mansoni. *J Infect Dis* 185, 98-105.

Deelder A.M., Kornelis D., Van Marck E.A., Eveleigh P.C. and Van Egmond J.G. (1980) Schistosoma mansoni: characterization of two circulating polysaccharide antigens and

the immunological response to these antigens in mouse, hamster, and human infections. *Exp Parasitol* 50, 16-32.

Digeon M., Droz D., Noel L.H., Riza J., Rieumailhol C., Bach J.F., Santoro F. and Capron A. (1979) The role of circulating immune complexes in the glomerular disease of experimental hepatosplenic schistosomiasis. *Clin Exp Immunol* 35, 329-337.

Doehring-Schwerdtfeger E., Abdel-Rahim I.M., Kardorff R., Kaiser C., Franke D., Schlake J., Richter J., Elsheikh M., Mohamed-Ali Q. and Ehrich J.H. (1992) Ultrasonographical investigation of periportal fibrosis in children with Schistosoma mansoni infection: reversibility of morbidity twenty-three months after treatment with praziquantel. *Am J Trop Med Hyg* 46, 409-415.

Doenhoff M., Musallam R., Bain J. and McGregor A. (1978) Studies on the host-parasite relationship in Schistosoma mansoni-infected mice: the immunological dependence of parasite egg excretion. *Immunology* 35, 771-778.

Doumenge J.P., Mott K.E., Cheung C., Villenave D., Chapuis O., Perrin M.F. and Reaud-Thomas G. (1987) *Atlas of the global distribution of schistosomiasis*. Geneva: Presses Universitaires de Bordeaux, Centre d'Etudes de Geographie Tropicale (C.N.R.S.)/World Health Organization.

Dunn M.A. and Kamel R. (1981) Hepatic schistosomiasis. *Hepatology* 1, 653-661.

Dunne D.W., Hagan P. and Abath F.G. (1995) Prospects for immunological control of schistosomiasis. *Lancet* 345, 1488-1491.

Dunne D.W. and Pearce E.J. (1999) Immunology of hepatosplenic schistosomiasis mansoni: a human perspective. *Microbes Infect* 1, 553-560.

El-Khoby T., Galal N., Fenwick A., Barakat R., El-Hawey A., Nooman Z., Habib M., Abdel-Wahab F., Gabr N.S., Hammam H.M., Hussein M.H., Mikhail N.N., Cline B.L. and Strickland G.T. (2000) The epidemiology of schistosomiasis in Egypt: summary findings in nine governorates. *Am J Trop Med Hyg* 62, 88-99.

Engels D., Sinzinkayo E. and Gryseels B. (1996) Day-to-day egg count fluctuation in Schistosoma mansoni infection and its operational implications. *Am J Trop Med Hyg* 54, 319-324.

Etard J.F., Audibert M. and Dabo A. (1995) Age-acquired resistance and predisposition to reinfection with Schistosoma haematobium after treatment with praziquantel in Mali. *Am J Trop Med Hyg* 52, 549-558.

Ezzat E., Tohamy M., El-Sherif A. and Omar A.H. (1978) Immunopathological study of glomerulonephritis associated with Schistosoma haematobium infection. *Proc Int Conf Schistosomiasis* 1, 625-628.

Fallon P.G., Sturrock R.F., Niang A.C. and Doenhoff M.J. (1995) diminished susceptibility to praziquantel in a Senegal isolate of Schistosoma mansoni. *Am J Trop Med Hyg* 53, 61-62.

Feldmeier H., Leutscher P., Poggensee G. and Harms G. (1999) Male genital schistosomiasis and haemospermia. *Trop Med Int Health* 4, 791-793.

Goldsmid J., Kibel M.A. and Mills A.E. (1998) *Forfar and Arneil's textbook of paediatrics*, 5th edi ed. Edinburgh: Churchill Livingstone.

Grimaud J.A. (1987) Cell-matrix interactions in schistosomal portal fibrosis: a dynamic event. *Mem Inst Oswaldo Cruz* 82 Suppl 4, 55-65.

Grzych J.M., Pearce E., Cheever A., Caulada Z.A., Caspar P., Heiny S., Lewis F. and Sher A. (1991) Egg deposition is the major stimulus for the production of Th2 cytokines in murine schistosomiasis mansoni. *J Immunol* 146, 1322-1327.

Hagan P., Blumenthal U.J., Chaudri M., Greenwood B.M., Hayes R.J., Hodgson I., Kelly C., Knight M., Simpson A.J., Smithers S.R. and et al. (1987) Resistance to reinfection with Schistosoma haematobium in Gambian children: analysis of their immune responses. *Trans R Soc Trop Med Hyg* 81, 938-946.

Hang L.M., Warren K.S. and Boros D.L. (1974) Schistosoma mansoni: antigenic secretions and the etiology of egg granulomas in mice. *Exp Parasitol* 35, 288-298.

Hillyer G.V. and Lewert R.M. (1974) Studies on renal pathology in hamsters infected with Schistosoma mansoni and S. japonicum. *Am J Trop Med Hyg* 23, 404-411.

Hood A.T. and Boros D.L. (1980) The effect of splenectomy on the pathophysiology and egg-specific immune response of Schistosoma mansoni-infected mice. *Am J Trop Med Hyg* 29, 586-591.

Houba V. (1979) Experimental renal disease due to schistosomiasis. *Kidney Int* 16, 30-43.

Houba V., Sturrock R.F. and Butterworth A.E. (1977) Kidney lesions in baboons infected with Schistosoma mansoni. *Clin Exp Immunol* 30, 439-449.

Hunter J.M., Rey L., Chu K.Y., Adekolu-John E.O. and Mott K.E. (1993) Parasitic diseases in water resource management: the need for intersectoral recognition. England: World Health Organization.

Ibelgauft H. (2008) Cytokines and cells online pathfinder encyclopaedia. In *Horst Ibelgaufts' cope.*

Ishak K.G., Legolvan, P.C., El-Sebai, I. (1967) *Malignant bladder tumours asssociated with shistosomiasis. A gross and microscopic study, in bilharziasis*. New York, Berlin: Springer-Velag.

Ishii A., Matsuoka H., Aji T., Ohta N., Arimoto S., Wataya Y. and Hayatsu H. (1994) Parasite infection and cancer: with special emphasis on Schistosoma japonicum infections (Trematoda). A review. *Mutat Res* 305, 273-281.

Jassim A., Catty D. and Hassan K. (1987) Antibody isotypes of immune complexes in schistosomiasis mansoni in Sudan. *Parasite Immunol* 9, 651-665.

Jeans A.K. and Schwellnus M.P. (1994) The risk of schistosomiasis in Zimbabwean triathletes. *S. Afr. Med. J.* 84, 756-758.

Katz N., Chaves A. and Pellegrino J. (1972) A simple device for quantitative stool thick-smear technique in Schistosomiasis mansoni. *Rev Inst Med Trop Sao Paulo* 14, 397-400.

King C.H. (2009) Toward the elimination of schistosomiasis. *N Engl J Med* 360, 106-109.

Lambertrucci J.R., Godoy P., Neves J., Bambirra E.A. and Ferreira M.D. (1988) Glomerulonephritis in Salmonella-Schistosoma mansoni association. *Am J Trop Med Hyg* 38, 97-102.

Lewert R.M. and Mandlowitz S. (1969) Schistosomiasis: prenatal induction of tolerance to antigens. *Nature* 224, 1029-1030.

Madwar M.A. and Voller A. (1975) Circulating soluble antigens and antibody in schistosomiasis. *Br Med J* 1, 435-436.

Mahmoud A.A.F. (2001) *Harrison's principles of internal medicine*, 15th ed: McGraw-Hill medical publishing.

Martindale (1993) *The extra pharmacopoeia*, 30th edition ed. London, England: The pharmaceutical press.

Masaba S.C., Awiti I.E. and Muruka J.F. (1983) Morbidity in urinary schistosomiasis in relation to the intensity of infection in Kisumu, Kenya. *J Trop Med Hyg* 86, 65-66.

MOH-GHS (2007-2008) Two year strategic plan for integrated neglected tropical diseases control in Ghana. 13.

Mohamed-Ali Q., Doehring-Schwerdtfeger E., Abdel-Rahim I.M., Schlake J., Kardorff R., Franke D., Kaiser C., Elsheikh M., Abdalla M., Schafer P. and et al. (1991)

Ultrasonographical investigation of periportal fibrosis in children with Schistosoma mansoni infection: reversibility of morbidity seven months after treatment with praziquantel. *Am J Trop Med Hyg* 44, 444-451.

Moriearty P.L. and Brito E. (1977) Elution of renal antischistosome antibodies in human schistosomiasis mansoni. *Am J Trop Med Hyg* 26, 717-722.

Natali P.G. and Cioli D. (1974) Immune complex nephritis in mice infected with *S. mansoni*. *Fed Proc* 33, 757-761.

Nkegbe E. (2010) Prevalence of schistosomiasis among school children in the lower River Volta basin in Ghana. *Gomal Journal of medical Sciences* 8, 54-56.

Nsowah-Nuamah N.N., Mensah G., Aryeetey M.E., Wagatsuma Y. and Bentil G. (2001) Urinary schistosomiasis in southern Ghana: a logistic regression approach to data from a community-based integrated control program. *Am J Trop Med Hyg* 65, 484-490.

Odei M.A. (1995) Scistosomiasis in Ghana. An overview paper presented at the seminar on "Schistosomiasis and EPI vaccine trials in Ghana" at Noguchi Memorial Institute for medical research, University of Ghana, Legon.

Ogunba E.O., Maddison S.E., Tsang V.C. and Slemenda S.B. (1982) Reactivity of fractionated egg antigens of Schistosoma mansoni with sera of patients infected with S. haematobium. *Afr J Med Med Sci* 11, 67-73.

Okanla E.O., Agba B.N. and Awotunde J.O. (2003) Shistosoma haematobium: Prevalence and socio-economic factors among students in Cape Coast Ghana. *African Journal of Biomedical Research* 6, 69-72.

Paperna I. (1969) Studies on the transmission of schistosomiasis in Ghana: V. Transmission of *Schistosoma haematobium* in the forest and savannah zones of South East Ghana. *Ghana Med J.* 8, 35-46.

Paul J.F., Verma S. and Berry K. (2002) Urinary schistosomiasis. *Emerg Med J* 19, 483-484.

Pearce E.J., Caspar P., Grzych J.M., Lewis F.A. and Sher A. (1991) Downregulation of Th1 cytokine production accompanies induction of Th2 responses by a parasitic helminth, Schistosoma mansoni. *J Exp Med* 173, 159-166.

Pearce E.J. and MacDonald A.S. (2002) The immunobiology of schistosomiasis. *Nat Rev Immunol* 2, 499-511.

Phillips S.M. and Lammie P.J. (1986) Immunopathology of granuloma formation and fibrosis in schistosomiasis. *Parasitol Today* 2, 296-302.

Poggensee G., Krantz I., Kiwelu I., Diedrich T. and Feldmeier H. (2001) Presence of Schistosoma mansoni eggs in the cervix uteri of women in Mwanga District, Tanzania. *Trans R Soc Trop Med Hyg* 95, 299-300.

Rocha H., Cruz T., Brito E. and Susin M. (1976) Renal involvement in patients with hepatosplenic Schistosomiasis mansoni. *Am J Trop Med Hyg* 25, 108-115.

Ross A.G., Bartley P.B., Sleigh A.C., Olds G.R., Li Y., Williams G.M. and McManus D.P. (2002) Schistosomiasis. *N Engl J Med* 346, 1212-1220.

Sabah A.A., Fletcher C., Webbe G. and Doenhoff M.J. (1986) Schistosoma mansoni: chemotherapy of infections of different ages. *Exp Parasitol* 61, 294-303.

Salih S.Y., Subaa H.A., Asha H.A. and Satir A.A. (1977) Salmonellosis complicating schistosomiasis in the Sudan. *J Trop Med Hyg* 80, 14-18.

Santoro F., Carlier Y., Borojevic R., Bout D., Tachon P. and Capron A. (1977) Parasite 'M' antigen in milk from mothers infected with Schistosoma mansoni (preliminary report). *Ann Trop Med Parasitol* 71, 121-123.

Scherrer A.U., Sjoberg M.K., Allangba A., Traore M., Lohourignon L.K., Tschannen A.B., N'Goran E.K. and Utzinger J. (2009) Sequential analysis of helminth egg output in human stool samples following albendazole and praziquantel administration. *Acta Trop* 109, 226-231.

Shaw M.K. (1990) Schistosoma mansoni: stage-dependent damage after in vivo treatment with praziquantel. *Parasitology* 100 Pt 1, 65-72.

Steinmann P., Keiser J., Bos R., Tanner M. and Utzinger J. (2006) Schistosomiasis and water resources development: systematic review, meta-analysis, and estimates of people at risk. *Lancet Infect Dis* 6, 411-425.

Taylor M.G., Nelson G.S., Smith M. and Andrews B.J. (1973) Comparison of the infectivity and pathogenicity of six species of African schistosomes and their hybrids. 2. Baboons. *J Helminthol* 47, 455-485.

Useh M.F. and Ejezie G.C. (1999) Modification of behaviour and attitude in the control of schistosomiasis. 1. Observations on water-contact patterns and perception of infection. *Ann Trop Med Parasitol* 93, 711-720.

Utzinger J., Booth M., N'Goran E.K., Muller I., Tanner M. and Lengeler C. (2001) Relative contribution of day-to-day and intra-specimen variation in faecal egg counts of Schistosoma mansoni before and after treatment with praziquantel. *Parasitology* 122, 537-544.

van der Werf M.J., de Vlas S.J., Brooker S., Looman C.W., Nagelkerke N.J., Habbema J.D. and Engels D. (2003) Quantification of clinical morbidity associated with schistosome infection in sub-Saharan Africa. *Acta Trop* 86, 125-139.

Van March E., Deelder A.M. and Gigase P.L.G. (1977) Effect of portal vein ligation on immune glomerular deposits in schistosoma mansoni infected mice. *Br J Exp pathol* 58, 412-417.

Von Lichtenberg F., Sadun E.H., Cheever A.W., Erickson D.G., Johnson A.J. and Boyce H.W. (1971) Experimental infection with Schistosoma japonicum in chimpanzees. *Am J Trop Med Hyg* 20, 850-893.

Warren K.S. (1982) Schistosomiasis: host-pathogen biology. *Rev Infect Dis* 4, 771-775.

Warren K.S., Mahmoud A.A., Muruka J.F., Whittaker L.R., Ouma J.H. and Arap Siongok T.K. (1979) Schistosomiasis haematobia in coast province Kenya. Relationship between egg output and morbidity. *Am J Trop Med Hyg* 28, 864-870.

WHO (1985) The control of schistosomiasis: Report of a WHO expert committee. In *WHO Technical Report Ser 728*.

WHO (1993) The control of schistosomiasis. In *WHO Technical Report Series 830*. Geneva: World Health Organization.

WHO (2002) Prevention and control of schistosomiasis and soil transmitted helminthiasis. WHO Expert Committee, pp. 1-57.

Wyler D.J. (1983) Cytopathology of parasitic disease. *Ciba Found Symp* 99, 190-206.

Xiao S.H., Catto B.A. and Webster L.T., Jr. (1985) Effects of praziquantel on different developmental stages of Schistosoma mansoni in vitro and in vivo. *J Infect Dis* 151, 1130-1137.

APPENDIX

Appendix 1

QUESTIONNAIRE FOR SELECTION OF PARTICIPANTS FOR SAMPLING

Title of research:

Epidemiology of *Schistosoma haematobium* and *Schistosoma mansoni* infections among school children in the Kassena/Nankana West District of Ghana: pre- and post treatment with praziquantel

Name_____

Age_____ Sex_____

Name of parent/ guardian _____

House number_____

Answer YES or NO

1. Do you have any contact with water bodies (dams, rivers, etc)? _____
2. Do you work on the farms? _____
3. If yes, do you use irrigation methods on the farm? _____
4. Do you experience weakness? _____
5. Did you have blood in your urine during the last month? If yes, when? _____
6. Do you have blood in your stool? If yes, when? _____
7. Do you have past history of schistosomiasis infection? If yes, when? _____
8. Have you been previously treated for schistosomiasis? If yes, when? _____

Appendix 2

CONSENT FORM

Statement of person obtaining informed consent:

I have fully explained this research to _____ and have given sufficient information, including that about risks and benefits, to enable the prospective participant make an informed decision to or not to participate.

DATE: _____ SIGNATURE: _____

NAME: _____

Statement of person giving consent:

I have read the information on this study/research or have had it translated into a language I understand. I have also talked it over with the interviewer to my satisfaction. I understand that my wards participation is voluntary (optional). I know enough about the purpose, methods, risks and benefits of the research study to judge that I want my ward to take part in it. I understand that my ward may freely stop being part of this study at any time. I have received a copy of this information leaflet and consent form to keep for myself.

Name _____

DATE: _____ SIGNATURE/THUMB PRINT: _____

RELATIONSHIP TO PARTICIPANT: _____

WITNESS' SIGNATURE: _____

WITNESS' NAME: _____