PREVALENCE OF LIVER DISEASE IN *SCHISTOSOMA MANSONI* INFECTION IN SIAVONGA DISTRICT OF ZAMBIA

By

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A dissertation submitted to the University of Zambia in partial fulfillment of the requirements for the Degree of Master of Science in Parasitology.

The University of Zambia, Lusaka

2010

DECLARATION

This dissertation represents the original work of MR RICHARD BANDA. It has been done in accordance with the guidelines for the Master of Science in Medical Parasitology dissertation of the University of Zambia. It has not previously been submitted for a degree, diploma or other qualification at this University or any other institution and the contents are of my own work.

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ABSTRACT

The Siavonga District in the Southern Province has one of the highest prevalence of schistosomiasis in Zambia. The objective of this community based cross-sectional study was to determine the prevalence of liver disease due to *Schistosoma mansoni* infection amongst the population of Game Village, Siavonga District. The study was carried out from June to October 2007 on 269 individuals who were asked to submit stool and urine samples for schistosomiasis examination. Clinical, laboratory and ultrasound examinations, including the Knowledge, Attitude and Practices (KAP) questionnaire, were used to collect data. The prevalence of *S. mansoni* infection found on 269 study participants examined was 175 or 65% and was the most prevalent infections. Of the 175 cases of *S. mansoni* infections found, 61% were light infections, 34% were moderate infections and 5% were heavy infections. It was found that children had a higher chance of contracting schistosomiasis than adults. It was further noticed that females had a higher chance of contracting schistosomiasis because of the nature of activities they perform than males. The prevalence of liver disease due to *S. mansoni* infection as confirmed by microscopic examination of stool samples and ultrasound was 6 cases or 3.4% and mostly observed in the young between 12 to 24 years old regardless of the intensity of infection.

ACKNOWLEDGEMENTS

This project would not have been possible without the support of many people. Many thanks go to my supervisor, Dr Cecilia. J Shinondo, Head of Biomedical Sciences, School of Medicine, University of Zambia, my co-supervisor, Dr Enala Mwase, Department of Para-Clinical Studies, School of Veterinary Sciences, University of Zambia, for providing good guidance and support. Thanks to the University of Zambia for providing a conducive learning environment and necessary facilities. Many thanks go to the National Institute for Scientific and Industrial Research (NISIR) for awarding me study leave to pursue a Master of Science degree course and for providing financial support to accomplish my studies. I am also grateful to DANIDA for granting me Water Research Fund for Southern Africa (WARFSA) funds for my Research work. Iam very grateful to Dr J. C. L. Mwansa, consultant microbiologist at UTH and chairperson of the Zambia Bilharzia Control Programme (ZBCP) for guidance, financial and material support and for allowing me to use their equipment in the field during data collection exercise. Finally, many thanks go to my wife Silvia Banda, my son Tionge Banda, and my beloved late daughter Kondwani Banda who died at the age of 13 during the time when I begun collecting data for my dissertation writing. She was a source of happiness to all of us. We cherished her and shall greatly miss her. May her soul rest in eternal peace. Thanks also go to my parents and numerous friends who endured this long process with me, always offering support and love. May the good Lord bless you.

DEDICATION

This dissertation is dedicated with deep feelings to my family members who are my pillars for their patience during this long process of waiting for me as I pursued studies.

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LIST OF ABBREVIATIONS

APPF-Advanced Periportal fibrosis

SCI-Schistosomiasis Control Initiative

HIV-Human immunodeficiency virus

KAP-Knowledge, Attitudes and Practices

MCL-Mid clavical line

MAL-Mid axillary line

PSL-Liver parasternal line

WHO-World Health Organization

GIT- Gastro intestinal tract

DALYs- Disability Adjusted Life Years

Epg- Eggs per gram of stool

GMEC- Geometric Mean Egg Count

EPPF- Early periportal fibrosis

MPPF- Moderate periportal fibrosis

STDEV- Standard deviation

MLNE- Monocytes, Lymphocytes, Neutrophils and Eosinophils

WARFSA- Water research fund for Southern Africa

NISIR- National Institute for Scientific and Industrial Research

DANIDA- Danish International Development Agency

ZBCP- Zambia Bilharzia Control Programme

MoH- Ministry of Health

CHAPTER 1.0 INTRODUCTION

1.1 Background

Schistosomiasis or bilharzia is a disease affecting many people in the developing countries and is one of the major parasitic diseases of huge public health importance today. It is considered the second most important human parasitic diseases after malaria in terms of morbidity and mortality (Chitsulo *et al*, 2000). In many areas within sub-Saharan Africa, it continues to drain the socio-economic development of already impoverished rural communities. Bilharzia or bilharziosis is the eponym for schistosomiasis after Theodor Bilharz, who first described the cause of urinary schistosomiasis in 1851 (Jordan and Webbe, 1982).

There are five species of flatworms that cause schistosomiasis. Each species causes a different clinical presentation of the disease. Schistosomiasis may localize in different parts of the body and its localization determines its particular clinical profile (Jordan *et al*, 1993). *Schistosoma mansoni* and *Schistosoma intercalatum* cause intestinal schistosomiasis. *Schistosoma haematobium* causes urinary schistosomiasis. *Schistosoma japonicum* and *Schistosoma mekongi* cause Asian intestinal schistosomiasis (Caatinga *et al*, 2000).

Schistosomes have a typical trematode vertebrate-invertebrate life cycle, with humans being the definitive host. The life cycles of all five human schistosomes are broadly similar. The most common way of getting schistosomiasis is by wading or swimming in lakes, ponds and other bodies of water which are infested with the snails (usually of the *Biomphalaria*, *Bulinus*, or *Oncomelania* genus) that are the natural reservoirs of the schistosomiasis pathogen (Caatinga *et al*, 2000).

Parasite eggs are released into the environment from infected individuals, hatching on contact with fresh water to release the free-swimming miracidium. Miracidia infect fresh-water snails by penetrating them. After infection, close to the site of penetration, the miracidium transforms into a primary (mother) sporocyst. Germ cells within the primary sporocyst then begin dividing to produce secondary (daughter) sporocysts,

which migrate to the snail's hepatopancreas. Once at the hepatopancreas, germ cells within the secondary sporocyst begin to divide again, this time producing thousands of new parasites, known as cercariae, which are the larvae capable of infecting mammals. Cercariae emerge daily from the snail host in a circadian rhythm, dependent on ambient temperature and light. Young cercariae are highly motile, alternating between vigorous upward movements and sinking to maintain their position in the water. Cercarial activity is particularly stimulated by water turbulence, shadows and human skin chemicals (Andrade and Bina, 1983).

Penetration of the human skin occurs after the cercaria have attached to the exposed skin. The parasite secretes enzymes that break down the skin to enable penetration of the cercarial head. As the cercaria penetrates the skin it transforms into a migrating schistosomulum stage. The newly transformed schistosomulum may remain in the skin for 1-2 days before locating a post-capillary venule where the schistosomulum travels to the lungs and it undergoes further developmental changes necessary for subsequent migration to the liver. Eight to ten days after penetration of the skin, the parasite migrates to the liver sinusoids. *S. japonicum* migrates more quickly than *S. mansoni*, and usually reaches the liver within 6-8 days of penetration. Juvenile *S. mansoni* and *S. japonicum* worms develop an oral sucker after arriving in the liver, and it is during this period that the parasite begins to feed on red blood cells. The nearly-mature worms pair, with the longer female worm residing in the gynaecophoric channel of the male. Adult worms are about 10 mm long. Worm pairs of *S. mansoni* and *S. japonicum* relocate to the mesenteric or rectal veins. *S. haematobium* schistosomula ultimately migrate from the liver to the perivesical venous plexus of the bladder, ureters and kidneys through the haemorrhoidal plexus. Parasites reach maturity in 6-8 weeks, at which time they begin to produce eggs. Adult *S. mansoni* pairs residing in the mesenteric vessels may produce up to 300 eggs per day during their reproductive lives. *S. japonicum* may produce up to 3000 eggs per day (Bina and Prata, 1990).

Many of the eggs pass through the walls of the blood vessels, and through the intestinal wall, to be passed out of the body in faeces. *S. haematobium* eggs pass through the

ureteral or bladder wall and into the urine. Only mature eggs are capable of crossing into the digestive tract, possibly through the release of proteolytic enzymes, but also as a function of host immune response, which fosters local tissue ulceration. Up to half the eggs released by the worm pairs become trapped in the mesenteric veins, or will be washed back into the liver, where they will become lodged. Worm pairs can live in the body for an average of four to five years, but may persist up to 20 years. Trapped eggs mature normally, secreting antigens that elicit a vigorous immune response. The eggs themselves do not damage the body. Rather, it is the cellular infiltration resultant from the immune response that causes the pathology classically associated with schistosomiasis (Bina and Prata, 1990).

The objective of this community based cross-sectional study was to determine the prevalence of liver disease due to *Schistosoma mansoni* infection amongst the population of Game Village in the Siavonga District. The study was carried out using clinical, laboratory and ultrasound examinations, including the Knowledge, Attitude and Practices (KAP) questionnaire to collect data. The study focused mainly on the prevalence of liver disease due to *Schistosoma mansoni* infection on the study population living in a schistosomiasis endemic area of the Game Village in the Siavonga District of Zambia.

1.2 Statement of the Problem

In Zambia about 2 million people are affected with schistosomiasis (MoH, 2006). The investigations carried out in the Siavonga District by Mubila and Robinson (2002) and Chimbari *et al*, (2003) found the prevalence of *Schistosoma mansoni* infection to be 32% respectively. Another study undertaken by the Schistosomasis Control Initiative (2007) in the Siavonga District found the prevalence of *Schistosoma mansoni* infection to be 77%.

The general signs and symptoms of gastro-intestinal tract (GIT) infections like abdominal pain, diarrhoea, abdominal enlargement and passing blood in stool are common in many cases. Despite the abdominal syndrome being common, the clinical

importance of *Schistosoma mansoni* infection has not been determined. No study has provided data on the prevalence of liver disease in school-children and adults infected with *Schistosoma mansoni* in the Siavonga District.

1.3 Justification of the Study

This study is new in this part of Zambia and the data that was collected and analysed was intended to be used to understand the clinical picture of the disease in the *Schistosoma mansoni* infected individuals. The parasitological examination of specimens and the assessment of knowledge, attitude and practices (KAP) questionnaire was important in that it provided an opportunity for designing intervention strategies in the management of the disease and putting in place long-term strategies for sustainable morbidity control.

1.4 Literature Review

Schistosomiasis is found in tropical countries in Africa, the Caribbean, Eastern South America, East Asia and in the Middle East. *Schistosoma mansoni* is found in parts of South America and the Caribbean, Africa, and the Middle East. *S. haematobium* is found in Africa and the Middle East and *S. japonicum* in the Far East. *S. mekongi* and *S. intercalatum* are found focally in Southeast Asia and Central West Africa, respectively. Although it has a low mortality rate, schistosomiasis can be very debilitating. About 600 million people are thought to be at risk of schistosomiasis infection and 200 million are estimated to be infected in 74 countries (Chan *et al*, 1996). One hundred and twenty million people have symptoms of passing eggs in stool and urine. Twenty million have symptoms of stunted growth, anaemia, and chronic ill health The current estimated total number of individuals with morbidity and mortality due to schistosomiasis infection in sub-Saharan Africa may be as high as 200 000 deaths per year due to non-functioning kidney and bladder cancer in respect of *Schistosoma haematobium* infection and haematemesis in case of *Schistosoma mansoni* infection.

Schistosomiasis is a chronic disease. The chronic forms of the disease are either intestinal or hepatosplenic. The intestinal form may have no symptoms, but blood in the

stools is the most common complaint in the absence of hepatosplenic involvement. Pathology of *S. mansoni* and *S. japonicum* schistosomiasis includes Katayama fever, hepatic perisinusoidal egg granulomas, symmers' pipe stem periportal fibrosis, portal hypertension, and occasional embolic egg granulomas in brain or spinal cord. Pathology of *S. haematobium* schistosomiasis includes haematuria, scarring, calcification, squamous cell carcinoma and occasional embolic egg granulomas in brain or spinal cord. Bladder cancer diagnosis and mortality are generally elevated in affected areas (Caatinga *et al*, 2000).

Many infections are subclinically symptomatic, with mild anaemia and malnutrition being common in endemic areas. Acute schistosomiasis (Katayama's fever) may occur weeks after the initial infection, especially by *S. mansoni* and *S. japonicum*. Manifestations include abdominal pain, cough, diarrhoea, eosinophilia, extremely high white blood cell count, fever, fatigue and hepatosplenomegaly. Occasionally central nervous system lesions occur. Cerebral granulomatous disease may be caused by ectopic *S. japonicum* eggs in the brain, and granulomatous lesions around ectopic eggs in the spinal cord from *S. mansoni* and *S. haematobium* infections may result in a transverse myelitis with flaccid paraplegia. Continuing infection may cause granulomatous reactions and fibrosis in the affected organs which may result in manifestations that include colonic polyposis with bloody diarrhoea (*Schistosoma mansoni* mostly), portal hypertension with haematemesis and splenomegaly (*S. mansoni*, *S. japonicum*; cystitis and ureteritis (*S. haematobium*) with haematuria which can progress to bladder cancer, pulmonary hypertension (*S. mansoni*, *S. japonicum*, more rarely *S. haematobium*), glomerulonephritis and central nervous system lesions (Caatinga *et al*, 2000).

Microscopic identification of eggs in stool or urine is the most practical method for schistosomiasis diagnosis. For the measurement of eggs in the faeces of presenting patients, the scientific unit used was eggs per gram of stool. Stool examination should be performed when infection with *S. mansoni* or *S. japonicum* is suspected and urine examination should be performed if *S. haematobium* is suspected. Eggs can be present in