BACTERIA IN PRIMARY SCHOOL CHILDREN WITH URINARY SCHISTOSOMIASIS IN RURAL COMMUNITIES IN ENUGU STATE, NIGERIA

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DECLARATION

I declare that the work in the dissertation entitled ‘ Bacteriuria in Primary School Children with Urinary Schistosomiasis in Rural Communities in Enugu State, Nigeria’ has been performed by me in the Department of Community Medicine under the supervision of Dr Turkur Dahiru. The information derived from the literature has been duly acknowledged in the text and a list of references provided. No part of this dissertation was previously presented for another degree or diploma at any university.

OKECHUKWU PAULINUS OSSAI **DATE--------------**

CERTIFICATION

I certify that the work for this dissertation entitled “BACTERIURIA IN PRIMARY SCHOOL CHILDREN WITH URINARY SCHISTOSOMIASIS IN RURAL COMMUNITIES IN ENUGU STATE, NIGERIA” by Dr. Okechukwu Paulinus Ossai meets the regulation governing the award of of the degree of Masters of Public health in Field Epidemiology of Ahmadu Bello University, Zaria and is approved for its contribution to knowledge and literary presentation

.... Date……………………

External Examiner

……………………… Date……………………

Internal Examiner

……………………….. Date…………………..

Head of Department

………………………... Date……………………

Dean, Postgraduate School

DEDICATION

This work is dedicated to my entire family who stood solidly behind me in the course of this study. Above all it is dedicated to my late brother Engr. Godwin Ossai who was not given the opportunity to reap the fruits of his labour.

ACKNOWLEDGMENTS

I would like to thank those who have contributed in making this study a success. My special appreciations go to all members of my family for their moral and financial support during the period of this study especially my wife, Mrs. Eugenia Ossai. I am also immensely grateful to my supervisor Dr. Turkur Dahiru for his patience, advice and diligent guidance throughout the period of this study.

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ACRONYMS

AIDS	Acquire Immune Deficiency Syndrome
HIV	Human Immune-Deficiency Virus
df	Degree Of Freedom
DSNO	Disease Surveillance and Notification Officer
ESUT	Enugu State University of Science and Technology
IDSR	Integrated Disease Surveillance and Response
LGA	Local Government Area
MDA	Mass Drug Administration
NPV	Negative Predictive Value
OR	Odds Ratio
PPV	Positive Predictive Value
SG	Specific Gravity
UTI	Urinary Tract Infection
WHO	World Health Organization
X^2	ChiSquare

ABSTRACT

Urinary schistosomiasis though being second to malaria as the most economically devastating disease is highly neglected in Nigeria. In fact it was only in 2010 that it was introduced into the Integrated Disease Surveillance and Response (IDSR). This has made the control of the disease more challenging despite its known high endemicity in the country. Several studies have shown that the disease can lead to some dangerous complications ranging from gross mental retardation in children to renal complications such as bladder cancer. In Enugu state haematuria is a common complaint in many communities. However, the only attempt to study and characterize the disease was in a focal community as far back as in 1989. No attempt has been made to establish the burden in the state or determine the factors that predispose to the infection and other associated complications.

We carried out a cross-sectional survey of primary school children between the ages of 5-15years who were randomly selected through a multi stage sampling method using WHO guidelines for schistosomiasis surveys. An interviewer administered questionnaire was used to collect data on demographic and socioeconomic variable, clinical presentations, risk factors. Urine samples were subjected to parasitological and bacteriology studies to determine prevalence, intensity as well as associated bacteria tract infections.

A urinary schistosomiasis pooled prevalence of 34.1% was established in the three LGAs surveyed. However some schools recorded higher prevalence. Heavy infections accounted for 62.7% and egg count per10mls of urine ranged from 21-1138 eggs/10mls urine. While haematuria gave the highest specificity and PPV, leucocyturia presented the highest sensitivity and NPV. The prevalence of associated bacteria urinary tract infection was 53.7% and the most implicated organism was

E.coli. Frequent visits to stream OR=6.92(4.74-10.14), closeness of open water body to household OR=5.7493.59-9.21), main source of water being open water bodies OR=11.49(7.00-19.03) were identified as risk factors to infection.

In conclusion, we have established that there is moderate prevalence of schistosomiasis in Enugu state (34.1%) which places it in category 2(20-50%) and therefore qualifies it for targeted mass drug administration in line with WHO guidelines. In the study, Haematuria with its high sensitivity and positive predictive value remains a very good marker for the diagnosis of urinary schistosomiasis especially at the community level. A high level of significant bacteriuria(53.7%) was also observed in our study far above the expected normal prevalence of 1-5%. This might spell doom for the state if positive action is not taken to control the menace.. In view of the above the state should carry out grass root sensitization of the rural populace especially on these identified risk factors to reduce fresh infections and re-infections. Identified cases should immediately be treated in line with WHO guidelines. The high prevalence of associated bacteriuria among cases underscores the need for concurrent antibiotics administration in order to prevent complications.

CHAPTER ONE

INTRODUCTION

1.1 Background

Schistosomiasis otherwise called bilharzia or bilharziosis or snail fever is a neglected tropical disease caused by a trematode of the genus schistosoma. It is one of the major public health problems facing developing countries. School-aged children are at the greatest risk especially within the teen age and boys are more affected than girls[1]. Infection is mostly found in Asia, Africa and South America in areas where the water contains fresh-water snails which carry the parasite.

Globally, over 600million people are at risk with over 200million infections in 74-76 countries. An estimated 20million people come down with the disease following infection and it is estimated that about 20,000 deaths are attributed to the disease annually[2]. Africa accounts for over 85% of the burden and it is estimated that over 477million persons are at risk in the continent.

Nigeria is the most endemic country in the world for urinary schistosomiasis with over 101.83million people being at risk and an estimated 25.83million people infected[3, 4].

Although many infections are asymptomatic, persons with infection in a resource constrained tropical areas of the world like Nigeria, usually present late with severe illness and after complications have developed[5]. In urinary schistosomiasis, haematuria, nutritional deficiencies, growth retardation and impaired cognitive development are common[6]. It may take up to 10-20 years after initial infection for terminal complications such as renal failure and squamous cell carcinoma of the bladder to develop[7, 8].

The debilitating nature of the disease is a markedly a cause of delay in school enrollment and poor performance, and low output in food and other production sectors. After many years of repeated infections, parasite can damage several organs resulting in diminished strength and production capacity among the people affected. They fail to go to school or work, which retards societal growth as is often observed in rice farming, sugar cane growing and fishing communities.

In schistosomiasis due to *S. haematobium*, the intensity of infection, or worm burden, is correlated with morbidity, the degree of haematuria and proteinuria, and the pathological changes observed in the urinary bladder and ureters,[9,10,11,12,13] and malignancies of the bladder[14] .

Generally, knowledge on the potential associations of the parasitic disease with other infectious diseases such as bacteria or viral infections is so far not well understood. The control measures instituted by various agencies pay little attention to the complexity of schistosomiasis morbidity and its assumed dependency on co-infection with bacteria due to dearth of knowledge in this area. Several biological factors have been implicated in predisposing individuals to the complications of urinary schistosomiasis such as bladder cancer. HIV and malaria with their impact on the immunologic system have been implicated[15]. Bacterial infections have also been fingered; with the mucosal barrier broken down, the urinary tract should be easy target for invading bacteria. Haematuria, proteinuria and leucocyturia indicate the damage induced by schistosomiasis eggs. These bacteria can accelerate the multi-stage process of bladder carcinogenesis as experimental evidence has shown by the formation of N-nitroso compounds, (some of which are known bladder carcinogens) produced from amine precursors and nitrate in urine during bacterial infections. Surprisingly, systematic knowledge about bacterial co-infection and schistosomiasis in this age group is scanty which is understandable since methods for schistosomiasis surveys are not optimal for detecting bacteruria[16]. Against this background, knowledge of the occurrence of urinary schistosomiasis as well as its associated bacteriuria, and types of bacteria prevalent in those cases are necessary for effective control of the disease and in preventing the impending complications. We investigated the current prevalence of urinary schistosomiasis and co-infection with bacteriuria in this state.

1.2 Problem Statement

Typically, schistosomiasis is a disease affecting agricultural communities. It is estimated that over 70% of the population of Enugu state are involved in subsistence farming[17]. Their main farming activities includes, rice production, fishing and plantain/banana production which predispose people to infection with schistosomiasis. Previous study of the burden of schistosomiasis in one community in the state in 1989 gave a high prevalence of 79%[18].This result is only from a community in the state and cannot be generalized. Moreover the information is too old to be used for present day decision making. There is also no knowledge on the co-infection with bacteriuria. However, there are frequent reports of haematuria (urine poison) from rural communities.

1.3 Justification

Recently studies have implicated co-infection with bacteriuria in the aetiology of bladder cancer. Unfortunately knowledge about co-infection of bacteriuria and urinary schistosomiasis in this age group(5-15years) who are mostly at risk is not available in the state and no major attempt has been made to establish the prevalence of urinary schistosomiasis in other parts of the state till date. The only attempt was the study done in one focal community in 1989 where a prevalence of 79% was documented[18].

Studies from other parts of the world indicate that co- infections of urinary schistosomiasis with bacteriuria continues to be a widespread problem and although their immediate impact on an individual may seem slight, the long term complication is a major health care challenge. Many studies also point out that a lot of work still needs to be done to gain more knowledge on the association between schistosomiasis and bacteria urinary tract infection and to harness such information for a comprehensive programme management and in preventing impending complications. Furthermore, information on co-morbidity in children with urinary schistosomiasis will add knowledge to the complications of the disease.

1.4 Aim and Objectives

1.4.1 General Objective

To determine the prevalence of urinary schistosomiasis, risk factor for infection and the associated bacteria urinary tract infection (UTI) among primary school children in rural communities in Enugu state Nigeria

1.4.2 Specific Objectives

1. To determine the prevalence of urinary schistosomiasis and associated risk factors among primary school children in rural communities in Enugu state Nigeria
2. To determine the prevalence of bacteria urinary tract infection among primary school children with urinary schistosomiasis in rural communities in Enugu state Nigeria
3. To asses and compare the sensitivity of morbidity markers in diagnosis of schistosomiasis (haematuria, proteinuria, turbidity, leucocyturia and specific gravity)

CHAPTER TWO

LITERATURE REVIEW

2.1 History of Schistosomiasis

Even though the symptoms of schistosomiasis have been recognized for a very long time, the causative agent was however only described in 1951. Schistosoma eggs have been recovered from Chinese and Egyptian mummies showing that the infection was present in both of these early civilizations of mankind. This was first noted as early as 1910 by Sir Armand Ruffer who found calcified eggs in the kidneys of two mummies of the twentieth dynasty. This is further illustrated by the identification of hieroglyphics in the "Papyrus Elbers" which appear to refer to the disease, bloody urine (a typical symptom of infection with schistosoma haematobium) being frequently mentioned. Here this disease was mentioned by name hieroglyphics meaning dripping penis. Elsewhere in the Middle East, ancient Asyrian records also have reference to this disease which gave rise to bloody urine, showing knowledge of the disease was widespread even in ancient times. Also infection with related species of S. japonicum was recognized where it was known as Katayama disease in Far East.

Schistosomiasis known as bilharziasis or bilharziosis in many countries was named after Theodor Bilharz who first described the cause of urinary schistosomiasis in 1851. The first doctor who described the entire disease cycle was Piraja da Silva in 1908 as it was a common cause of death in ancient Egyptians in the Greco-Roman period. As at that period Egypt was noted to have the world's highest hepatitis co-infection rate linked to the use of unclean needles for the treatment of schistosomiasis by using tartar emetic.

Schistosoma was described in writings in the Gynaecological Papyrus of Kahun from 1900BC. Calcified ova have been found in Egyptian mummies from 1250BC

2.2 Burden and Distribution of schistosomiasis

Schistosomiasis is second only to malaria as the most socioeconomically devastating parasitic disease. Chronic schistosomiasis reduces the capacity of those infected to work and in some cases can result in death. In children, schistosomiasis can cause anaemia, stunting and a reduced ability to learn. It is estimated that over 200,000 deaths per year are due to schistosomiasis in sub-saharan Africa. Even at that, it is is being speculated that the burden of disease due to schistosomiasis is underestimated according to WHO Expert Committee on Prevention and Control of Schistosomiasis and soil transmitted helminthiasis which reviewed the recent data on morbidity and mortality due to schistosomiasis in sub-saharan Africa (Report of WHO Expert Committee, Geneva 2002. Ref: ISBN 92 4 120912 7)

Urinary schistosomiasis affects people of all age groups and is endemic in 53 countries, especially in the Middle East and Africa including the Islands of Madagascar and Mauritius. Schistosoma haematobium responsible for urinary schistosomiasis is the most prevalent and widespread species in Africa, Eastern Mediteranean and Middle East. Nigeria is the most endemic country in the world with an estimated 101.28 million people being at risk and 25.83 million infected. The disease is normally endemic in rice and sugar cane producing areas as well as fishing communities.

2.3 Population at Risk

School age children are most likely to become infected with this silent destructive disease because it is easily contracted while bathing or swimming in water contaminated with the parasite which is shed from snails and infects by penetrating human skin. However, schistosomiasis also can be transmitted simply through contact with contaminated water while performing daily chores such as washing laundry, fetching water and herding animals. Children shoulder the majority of schistosomiasis' consequences especially poor growth and impaired cognitive function. For communities already burdened by poverty and ravaged by scourges such as malaria and HIV/AIDS, schistosomiasis is especially devastating. Other effects of the disease include anaemia, bladder dysfunction, kidney and liver disease and premature death.

2.4 Transmission

The disease is transmitted through contact with contaminated water while performing daily chores such as washing, laundry, fetching water and herding animals. Although the local swimming pool provides enjoyment to children, it is also the site of transmission of schistosomiasis- a parasitic disease transmitted by water snails (Bulinus globosus).

2.5 Life Cycle

Schistosomes are digenetic ie that mature adults reproduce sexually in the definitive host(man) and asexually in intermediate host(bulinu snail) (common to all trematodes or flukes). They are also diecious meaning that adult worms are sexually distinct and that male characteristic that separates them from other flukes). The life cycle differs from that of other trematodes in that humans become infected by penetration of cercariae through the skin rather than through oral ingestion. The parasite eggs are released into the environment from the urine of infected individuals. These eggs when they come in contact with water hatch into free-swimming miracidia (0.2mm long) which penetrate the foot of the bulinus snail. The miracidia transforms into primary/mother sporocyst. Germ cells within the primary sporocyst will then begin to divide to produce secondary (daughter) sporocysts which migrate to the snails' hepatopancreas. Once at the hepatopancreas, germ cells within the secondary sporocyst begin to divide again, now producing thousands of new parasites called cercariae (1mm long) which are the larvae capable of infecting mammals. Cercariae can survive for 48 hours in fresh water when they must attach to skin of a human or another host or die. They emerge daily from snail in a circadian rythym and this is dependent on ambient temperature and light. They develop to cercariae which takes 4-6weeks. The cercariae can then penetrate the skin by producing enzymes that breaks down the skin protein. It then transforms into schistosomolum which migrates through the skin vein to the pulmonary vessels. From the pulmonary vein the schistosomolum migrates to the portal vein where it develops into the adult worm within 8 to 10 days of skin penetration. Mating takes place in the liver before the adult worm migrates to the peri-vesical venous plexus of bladder, ureters and the kidneys. The maturity to adult form takes 6-8weeks at which time they begin to produce eggs. Schistosoma haematobium produces about 20-200 eggs which are ellipsoidal with terminal spines each day. The eggs are passed out of the body through the ureteral or bladder wall into the urine. As the eggs pass, they cause necrosis, ulceration and bleeding. Only about 50% of the eggs are released while the rest may embolize to different parts of the body. The average life span of an adult worm is 5-12 years.

2.6 Clinical Presentation

Most of the pathology associated with infection of schistosoma haematobium is due to immune responses to eggs that become trapped in the host tissue through cellular infiltration. Penetration of cercariae into the skin can result in mild itching and a papular dermatitis. Schistosomiasis is typically a chronic disease. Acute cases (katayama fever) are rare in infections of Schistosoma haematobium. The incubation period is 14-84 days. Most infections may remain asymptomatic. Eggs secreted by adult worms enter the circulation and lodge in organs to cause granulomatous reactions. The eggs of Schistosoma haematobium typically lodge in the urinary tract and cause dysuria and haematuria.

Clinical findings make possible the division of the disease in two phases. First is the acute phase, which includes cercarian dermatitis caused by the penetration of cercarias inside the skin and Katayama fever that may appear 3-7 weeks after an exposure, and is characterized by fever, anorexia, abdominal pain and headaches. The second phase is the chronic phase. Its clinical manifestations vary depending on the parasite localization and the load. Calcifications in the bladder may appear late in the disease. Recently the disease has been associated with increased risk of bladder cancer.

2.7 Diagnosis

The diagnosis is guided by the patient history in an endemic area. This evidence is confirmed by the presence of the Schistosoma haematobium ova in urine samples, serological tests (very useful where the disease transmission is low), vesical biopsy, studies of circulating antigen by the ELISA capture method and pelvic ultrasound.

The corner stone for the diagnosis of urinary schistosomiasis is microscopy. Schistosoma eggs are shed in urine in a circadian rhythm after the incubation period is attained. These eggs can be viewed under a microscope after concentration. Quantification is done through urine syringe filtration using a a neuclopore membrane. Since eggs are passed intermittently or in small amounts, their detection will be enhanced by repeated examinations. Infections can be characterized into light and heavy infections depending on the amount of eggs seen per 10mls of urine. Egg count of less than 50 in 10mls of urine is considered as light infection while above that is taken as heavy infection.

Serological tests are useful to diagnose light infection where egg shedding may not be consistent and in travelers and others who have not had schistosomiasis previously. However, antibody tests do not distinguish past and current infection. Sensitivity and specificity of this test vary according to the antigen preparation used and how the test is performed. A newly developed reagent strip assay for the diagnosis of schistosomiasis based on parasite antigen detection in urine of infected individuals has been evaluated. The test uses the principle of lateral flow through a nitrocellulose strip of the sample mixed with a colloidal carbon conjugate of a monoclonal antibody specific for *Schistosoma* circulating cathodic antigen (CCA)

The test is easy to perform and requires no technical equipment or special training. The stability of the strips and the conjugate in the dry format lasts for at least 3 months at ambient temperature in sealed packages, making it suitable for transport and use in areas where schistosomiasis is endemic. This assay can easily be developed to an end-user format.

Tissue biopsy (biopsy of the bladder) may demonstrate eggs when urine examination is negative.

2.8 Prevention

Primarily, preventive measures involve avoiding wading, swimming, or other contact with fresh water in disease-endemic areas. Filtering with fine-mesh filters, heating bathing water to 50^0C for 5 minutes, or allowing water to stand for at least 24 hours before use can reduce risk of infection in untreated piped water coming from fresh water sources that might contain cercarie. Chlorination of swimming pools also reduces the risk in of infection to swimmers.

Prevention is best accomplished by eliminating the water dwelling snails that are the natural reservoir of the disease. Acrolein, Copper sulfate and niclosamide can be used for this purpose. Recently it was observed that snail population can be controlled by introducing or augmenting existing crayfish populations. However this technique should be employed with caution.

Good/proper designing of dams and other irrigation helps in reducing the risk of infection.

Without sufficient funds for the provision of safe water, mobilization and education of affected communities as well as provision of sanitary facilities, such as latrines, schistosomiasis will remain a neglected disease in most of Nigeria and other sub-saharan countries.

2.9 Management

In most epidemiological settings, the intermediate host snails cannot be controlled by cost-effective interventions, and in the absence of a vaccine, schistosomiasis control largely relies on chemotherapy, with praziquantel as the drug of choice[19]. An important feature of the disease is its focal distribution[20]. This results in a patchy distribution of risk, and communities across a region or country do not attach the same importance to schistosomiasis. Praziquantel is therefore not required everywhere and proper targeting is crucial, given the limited resources and the many other problems facing primary health care systems in sub-Saharan Africa.

The first step in targeting health interventions is to map the disease geographically and rank it according to the risk of infection and morbidity. In 1987, the first attempt to systematically map schistosomiasis on a global scale resulted in the Atlas of the global distribution of schistosomiasis[5]. A more recent effort using geographical information systems highlighted the scarcity of data for Africa[21], and underscored the need for a rapid and inexpensive epidemiological assessment tool that can be fully integrated within existing administrative systems. Such a tool, relying on simple school questionnaires, was developed more than a decade ago for schistosoma *haematobium* and has since been validated in a variety of ecological, epidemiological, and socio-cultural settings across sub-Saharan Africa. More recently, the approach was extended to S. mansoni and its validity assessed in several large-scale studies. Resources for controlling the parasite can thus be allocated in a more cost-effective way[22].

Another possibility is to define an intervention threshold, such as the prevalence of reported blood in urine of >30% (which often corresponds to an S. haematobium infection prevalence of >50%). When prevalence exceeds 50%, all schools or communities would benefit from specific control measures, for example, universal treatment with praziquantel. Schistosomiasis can be controlled by one of the great miracle medical discoveries of the 1980s the oral medicine praziquantel. The costs of this medicine have dropped from more than $2 per dose to 18cents and so great strides can be made in treating schistosomiasis. Studies of those treated show that within six months of receiving a dose of praziquantel up to 90 percent of the damage due to the schistosomiasis infection can be reversed. Urinary schistosomiasis is readily treated using a single dose of the drug praziquantel annually[19].

A single dose oral anti-helminthic treatment can also be given to pregnant and lactating women, but, as a general rule, drugs should not be given in the first trimester of pregnancy[7].

Due to the risk of re-infection from continuous contact with contaminated water bodies, WHO recommended that people who qualify for universal treatment should be given mass drug administration every 6 months, those for targeted treatment; every 1-2 years while those for selective treatment should be given every 2 year. Post intervention evaluation should be carried out 2 years after drug administration.

2.9.1 Different Chemotherapeutic agents used for urinary schistosomiasis:

Chemotherapy is targeted especially at school age children. The assumption is that reducing the worm burden in childhood when infection intensity is highest will prevent most long term complications occurring later in adulthood.

Several drugs have been used or tried for the treatment of urinary schistosomiasis and later abandoned because of poor effect or adverse reactions: antimonials, niridazole, lucanthone, hycanthone, oltipraz, cyclosporin A, levamisole, and oxamniquine.

Current treatment options are limited to praziquantel and metrifonate

2.9.1.1 Praziquantel

Praziquantel is the only drug on the WHO Model List of Essential Medicines for treating schistosoma haematobium. The broad spectrum antschistosomal drug is effective against all schistosoma species although it is refractory against immature parasites. Praziquantel is administered orally at a standard dose of 40mg/kg body weight. The most common adverse effects are gastrointestinal, including abdominal pain, nausea, vomiting, and diarrhoea, and are usually mild and last less than 24 hours.

2.9.1.2 Metrifonate

Metrifonate was introduced as a drug for humans in the 1960s and has been used extensively to treat urinary schistosomiasis. The standard dose of 7.5 to 10mg/kg given three times at 14- day intervals has been used extensively and is mostly well tolerated. Adverse effects are mainly as a result of cholinergic stimulation and include fatigue, muscular weakness, tremor, nausea, vomiting, and bronchospasm. Its use has been limited after a suggestion that it was inferior clinically, economically, and operationally to praziquantel. Subsequently metrifonate was withdrawn from the WHO Model List of Essential Medicines.

Other drugs have potential as treatment options for urinary schistosomiasis, such as artemisinin derivatives, albendazole, and amoscanate. Albendazole is often administered together with praziquantel for simultaneous control of schistosomiasis and soil-transmitted helminthiasis.

2.9.1.3 Artemisinins

The antischistosomal activity of the artemisinins, such as artesunate and artemether, was discovered in the early 1980s. The artemisinins are active against the liver stages(immature) worms, while the invasive stages and adult worms are less susceptible to the drugs. Adverse effects are minor and last for less than 24hours. Artemisinin monotherapy may not be beneficial due to stage- specific activity, but combination with existing drugs effective against other stages(eg praziquantel) may improve therapeutic efficacy.

2.9.1.4 Albendazole

Albendazole is indicated for the treatment of a variety of worm infestations. In recent years it has been co-administered with praziquantel with the goal of simultaneously controlling schistosomiasis and soil-transmitted helminthiasis. Albendazole is administered orally (usually as single 400mg dose), and reported adverse effects include gastrointestinal upsets, headaches, and dizziness, while rash, fever, elevated liver enzymes occur less frequently. There have been reports of elevated liver enzymes, headaches, loss of hair, low levels of white blood cells (neutropenia), fever, and itching if taken at higher doses and/or for a long period of time.

2.9.1.5 Amoscanate

Amoscanate is a broad-spectrum antihelminthic drug that exhibits activity against all major human schistosome parasites, other systemic parasites and gastrointestinal nematodes (eg hookworm). It has been tested extensively in China using the locally produced equivalent called 'nithiocyaminum'. Toxicity in experimental animals was quite low and mutagenicity tests in bacteria gave negative results; however, mutagenic metabolites were detected in urine of mammals given amoscanate. It was abandoned because of concerns over liver toxicity and availability of better drugs such as praziquantel. It is possible that amoscanate may represent a unique, broad-spectrum schistosomicide with the appropriate structural modifications to decrease liver toxicity.

2.10 Global Control of schistosomiasis

The first step in targeting health interventions is to map the disease geographically and rank it according to the risk of infection and morbidity. In 1987, the first attempt to systematically map schistosomiasis on a global scale resulted in the Atlas of the global distribution of schistosomiasis[5]. More recent effort using geographical information systems highlights the scarcity of data for Africa[21], and underscored the need for a rapid and inexpensive epidemiological assessment tool that can be fully integrated within existing administrative systems. Such a tool, relying on simple school questionnaires, was developed more than a decade ago for schistosoma haematobium and has since been validated in a variety of ecological, epidemiological, and socio-cultural settings across sub-Saharan Africa. More recently, the approach was extended to S. mansoni and its validity assessed in several large-scale studies.

In 1996 WHO recommended that any programme aimed at controlling morbidity due to soil-transmitted helminthiasis or schistosomiasis should begin with a baseline survey.

- Baseline surveys provide a sound basis for estimating the present status and the need for intervention in a population.
- Baseline surveys produce essential data to guide the development of control programmes at national, regional or district levels.
- Follow-up surveys monitor the impact of a control programme. WHO assigns great importance to baseline and follow-up surveys of soil-transmitted

helminthiasis and schistosomiasis and assists Member States in planning and implementing control activities.

Furthermore, in 2006, WHO published a strategy for preventive chemotherapy in human schistosomiasis/ helminthiasis to guide countries in the implementation of this integrated approach to control neglected tropical diseases.[23]

Three strategies are recommended by World Health Organization (WHO) for the use of chemotherapy in the treatment of infections of schistosomiasis and soil-transmitted helminthiasis in the community:

- UNIVERSAL population level application of anthelminthic drug in which the community is treated irrespective of age, sex, infection status or other social characteristic employed when prevalence is >50%
- TARGETED group level application of anthelminthic drug where the group may be defined by age, sex or other social characteristic, irrespective of infection status, used when prevalence is between 20-40%
- SELECTIVE individual level application of anthelminthic drug where selection is based on diagnosis of current infection, when prevalence is <20%

2.11 Schistosomiasis Control Effort in Nigeria

The federal ministry of health conducted a qualitative questionnaire survey aimed at reporting urinary schistosomiasis to determine the crude distribution of schistosoma haematobium in the country in 1991[24]. As at 2008 only Plateau, Nasarawa, Delta, Ondo and Ekiti states have started quantitative mapping of urinary schistosomiasis using haeme reagent dipstick test on randomly selected school children 5- 14 years of age[25].

Since 1999 nearly 800,000 praziquantel treatments have been distributed in three states in Nigeria. Although the success is remarkable, the programme has reached only about half of the children in need in those areas. Unlike mectizan, the drug used to fight river blindness and albendazole used with mectizan to fight lymphatic filariasis, no company donates praziquantel on a large scale. So the distribution is limited. The country also treated a cumulative total of 2million people from 1999-2008. This is less than 1% of the estimated 101.28million persons believed to need the drug.

Despite the high endemicity of urinary schistosomiasis in Nigeria only minimal achievements have been recorded considering the few states that control activities have started; the reason being largely due to absence of scientific information on this disease. The problem was even compounded by the non-inclusion of schistosomiasis in the national integrated disease surveillance and response (IDSR) until 2010.

2.1.2 Bacteriuria (bacteria urinary tract infection (BUTI))

In healthy people, urine in the bladder is sterile- no bacteria or other infectious organisms are present. The tube that carries urine from the bladder out of the body urethra contains no bacteria or too few to cause an infection. However any part of the urinary tract can become infected. An infection anywhere along the urinary tract is called urinary tract infection (UTI). UTIs are classified as upper or lower according to where they occur. Lower UTIs are infections of the urethra, bladder and occasionally prostate. Upper UTIs involve kidneys, ureters. In paired organs eg kidneys, infections can be in one or both organs. UTI can occur in children as well as adults. UTIs are almost always caused by bacteria although some viruses, fungi and parasites can infect the urinary tract as well. More than 85% of UTIs are caused by bacteria from intestine or vagina. Bacterial infection of the lower urinary tract – the bladder and urethra are very common especially in young, sexually active women. E. coli is the commonest bacteria causing lower UTI.

Asymptomatic bacteriuria is a condition in which there is larger than normal numbers of bacteria in the urine but symptoms do not result. In UTIs, newborn and infants may have no symptoms other than fever, whereas older children have pain in the bladder region and a need to urinate frequently. Diagnosis is based on examination of urine. In infancy boys are more likely to develop UTIs. After infancy girls are much more likely to develop them due to short urethra. Uncircumcised boys (due to accumulation of bacteria on the fore skin) and young children with severe constipation also are more prone to UTIs. Circumcision lowers the risk of UTI by about 10times in infancy.

2.12.1 Pathophysiology of bacteriuria

The urinary tract is normally sterile. Uncomplicated UTI involves the urinary bladder in a host without underlying renal, metabolic, or neurologic diseases. Cystitis represents bladder mucosal invasion, most often by enteric coliform bacteria (eg, *Escherichia coli*) that inhabit the periurethral vaginal introitus and ascend into the bladder via the urethra.

In recurrent *E coli* UTIs, peak colonization rates of the periurethral area 2-3 days prior to the development of the symptoms of acute cystitis range from 46-90%. During this same period, asymptomatic bacteriuria rates increase from 7% to 70%.[26]

. Generally, urine is a good culture medium. This is known to be worse when there is parasite infection especially with blood ejection as in urinary schistosomiasis. Factors unfavorable to bacterial growth include a low pH (5.5 or less), a high concentration of urea, and the presence of organic acids derived from a diet that includes fruits and protein. Organic acids enhance acidification of the urine.

Frequent and complete voiding has been associated with a reduction in the incidence of UTI. Normally, a thin film of urine remains in the bladder after emptying, and any bacteria present are removed by the mucosal cell production of organic acids.

If the defense mechanisms of the lower urinary tract fail, upper tract or kidney involvement occurs and is termed pyelonephritis. Host defenses at this level include local leukocyte phagocytosis and renal production of antibodies that kill bacteria in the presence of complement.

In general, there are 3 main mechanisms responsible for UTIs:

- Colonization with ascending spread
- Hematogenous spread
- Periurogenital spread

2.12.2 Bacterial virulence

Uropathogenic bacteria, derived from a subset of fecal flora, have traits that enable adherence, growth, and resistance of host defenses. These traits facilitate colonization and infection of the urinary tract.

Adhesins are bacterial surface structures that enable attachment to host membranes. In *E coli* infection, these include both pili (ie, fimbriae) and outer-membrane proteins (eg, Dr hemagglutinin). P fimbriae , which attach to globoseries-type glycolipids found in the colon and urinary epithelium, are associated with pyelonephritis and cystitis and are found in many *E coli* strains that cause urosepsis.

Type 1 fimbriae bind to mannose-containing structures found in many different cell types, including Tamm-Horsfall protein (the major protein found in human urine). Whether this facilitates or inhibits uroepithelial colonization is the subject of some debate.

Other factors that may be important for *E coli* virulence in the urinary tract include capsular polysaccharides, hemolysins, cytotoxic necrotizing factor (CNF) protein, and aerobactins. Several Kauffman serogroups of *E coli* that contain these virulence factors may be more likely to cause UTIs, including O1, O2, O4, O6, O16, and O18.

Another example of bacterial virulence is the swarming capability of *Proteus mirabilis.* Swarming involves the expression of specific genes when these bacteria are exposed to surfaces such as catheters. This results in the coordinated movement of large numbers of bacteria, enabling *P mirabilis* to move across solid surfaces. This likely explains the association of *P mirabilis* UTIs with instrumentation of the urinary tract.

2.12.3 Host resistance

Most uropathogens gain access to the urinary tract via an ascending route. The shorter length of the female urethra allows uropathogens easier access to the bladder. The continuous unidirectional flow of urine helps to minimize UTIs, and anything that interferes with this increases the host's susceptibility to UTI. Examples of interference include volume depletion, sexual intercourse, urinary tract obstruction, instrumentation, use of catheters not drained to gravity, and vesicoureteral reflux.

Secretory defenses help promote bacterial clearance and prevent adherence. Secretory immunoglobulin A (IgA) reduces attachment and invasion of bacteria in the urinary tract.

Urine itself has several antibacterial features that suppress UTIs. Specifically, the pH, urea concentration, osmolarity, and various organic acids prevent most bacteria from surviving in the urinary tract.

2.12.4 Aetiology of bacteriuria

E coli causes 70-95% of both upper and lower UTIs. Various organisms are responsible for the remainder of infections, including *S saprophyticus*, *Proteus* species, *Klebsiella* species, *Enterococcus faecalis,* other Enterobacteriaceae, and yeast. Some species are more common in certain subgroups, such as *Staphylococcus saprophyticus* in young women.

Most complicated UTIs are nosocomial in origin. Increasingly, UTIs in patients in health care institutions and in those with frequent antibiotic exposure are caused by multidrug-resistant gram-negative pathogens, such as extended-spectrum beta-lactamase (ESBL) and carbapenemase producers. However, the prevalence of multidrug-resistant pathogens varies by locality.[27]

People who have preexisting urinary tract structural abnormalities or obstruction carry a higher risk of UTI. UTIs are common following renal transplantation, bladder irritation by schistosoma organism. Susceptibility is especially high following infestation.

Calculi related to UTIs most commonly occur in people who experience recurrent UTIs with *Proteus, Pseudomonas,* and *Providencia* species. Perinephric abscesses are associated most commonly with *E coli, Proteus* species, and *S aureus* but also may be secondary to *Enterobacter, Citrobacter, Serratia, Pseudomonas,* and *Klebsiella* species. More unusual causes include enterococci, *Candida* species, anaerobes, *Actinomyces* species, and *Mycobacterium tuberculosis.* Twenty-five percent of infections are polymicrobial.

2.12.5 *Epidemiology*

UTIs have been well studied in Sweden and other parts of Europe.[28] These studies have shown that 1 in 5 adult women experience a UTI at some point, confirming that it is an exceedingly common worldwide problem.

The epidemiology of UTI in the tropics is less well documented. UTIs appear to be common and associated with structural abnormalities. Chronic infection from *Schistosoma haematobium* disrupts bladder mucosal integrity and causes urinary tract obstruction and stasis. *Salmonella* bacteriuria, with or without bacteremia, is very common in patients with schistosomiasis.

2.12.6 Age- and sex-related demographics

Uncomplicated UTIs are much more common in women than men when matched for age. A study of Norwegian men aged 21-50 years showed an approximate incidence of 0.0006-0.0008 infections per person-year, compared with approximately 0.5-0.7 per person-year in similarly aged women in the United States.

The largest group of patients with UTI is adult women. The incidence of UTI in women tends to increase with increasing age. Several peaks above baseline correspond with specific events, including an increase in women aged 18-30 years (associated with coitus—so-called honeymoon cystitis—and pregnancy).

Rates of infection are high in postmenopausal women because of bladder or uterine prolapse causing incomplete bladder emptying; loss of estrogen with attendant changes in vaginal flora (notably, loss of lactobacilli), which allows periurethral colonization with gram-negative aerobes, such as *E coli;* and higher likelihood of concomitant medical illness, such as diabetes.

Of neonates, boys are slightly more likely than girls to present with UTI as part of a gram-negative sepsis syndrome. The incidence in preschool-aged children is approximately 2% and is 10 times more common in girls. UTI occurs in 5% of school-aged girls, but it is rare in school-aged boys.

2.12.7 *Prognosis*

Even with effective antibiotic treatment, the average duration of severe symptoms in people with UTI is somewhat longer than 3 days. Features that have been associated with a more prolonged course than average include a history of somatization, previous UTI, urinary frequency, and more severe symptoms at baseline.[29].

Although simple lower UTI (cystitis) may resolve spontaneously, effective treatment lessens the duration of symptoms and reduces the incidence of progression to upper UTI. Even with effective treatment, however, about 25% of women with cystitis will experience a recurrence.

Younger patients have the lowest rates of morbidity and mortality. Factors associated with an unfavorable prognosis include the following:

- Old age
- General debility
- Renal calculi or obstruction
- Recent hospitalization
- Urinary tract instrumentation or antibiotic therapy
- Diabetes mellitus
- Chronic nephropathy
- Sickle cell anemia
- Underlying cancer
- Intercurrent chemotherapy

The mortality associated with acute uncomplicated UTI appears to be negligible. In contrast, the morbidity in terms of quality of life and economic measures is tremendous. Each episode of UTI in a young person results in an average of 6.1 days of symptoms, 1.2 days of decreased class/work attendance, and 0.4 days in bed[30] . Nosocomial infections develop in about 5% of patients admitted to hospitals, and UTIs account for 40% of these infections. From 2-4% of these patients become bacteremic, with a mortality of 12.5%.

2.13 Urinary schistosomiasis, Bacteriuria and Bladder cancer:

Cancer of the urinary bladder is one of the most common human malignancies and the most frequent malignant neoplasm of the urinary tract[31]. In industrialized countries, bladder cancer is strongly linked to occupational and environmental exposures to chemical carcinogens and, in Europe, one half of male and one third of female cases may be attributed to smoking[32]. Aromatic amines represent a common factor among cigarette smoking, many occupational exposures and urinary bladder cancer: compounds such as 4-aminobiphenyl and 2-naphthylamine were among the first to be identified as human bladder carcinogens[33]. In contrast to western countries, the high incidence of bladder cancer seen in East Africa and the Middle East and other subtropical countries is associated with chronic urinary infection with *Schistosoma* haematobium[34-36]. Carcinoma of the urinary bladder is the most common malignancy among Egyptian males, accounting for 40% of total cancer incidence, whereas in females it ranks second to breast cancer[37].

In Egypt and other endemic countries, bladder cancer incidence is high in areas where the prevalence and intensity of Schistosoma haematobium infection is also high. Experimental evidence shows bladder carcinogenesis to be a multi-stage process which can be accelerated by many factors. N-nitroso compounds, some of which are known bladder carcinogens, can be formed from amine precursors and nitrate in urine during some bacterial infections. In experimental animals the growth of nitrosamine-induced urothelial cancers is accelerated by damage to the urothelium caused by S. haematobium infections, and by analogy in man this could account for the lower peak age of incidence of this cancer in endemic countries by comparison with Europe.

The etiology of bladder cancer arising in association with schistosome infection is thought to be multifactorial[15]. Most attention, however, has focused on the possible role of urinary chemical carcinogens, particularly the *N*-nitroso compounds, in this process[38]. Carcinogenic *N*-nitroso compounds or their metabolites are alkylating agents that can react with cellular DNA to form a wide range of adducts[40]. Although apparently innocuous, N7-alkylguanine lesions are used as monitors of exposure to *N*-nitroso compounds, in part because of their relatively high levels in DNA and also because their repair rate is very much slower than that of other pro-mutagenic and carcinogenic lesions such as O^6-alkylguanine[39]. Nitrosamines have been detected in urine from *S. haematobium*–infected patients including those with bladder cancer at levels significantly higher than in uninfected individuals[40,41].

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CHAPTER THREE

METHODOLOGY

3.1 Study Area

Enugu state is in the south- eastern part of Nigeria and share common boundaries with five other states; Abia to the south, Benue and Kogi to the north,Anambra to the west and Ebonyi to the east. The state has a population of 3.9 million projected from 2006 population census at a growth rate of 3.18%.

It has 3 senatorial zones, 17 local government areas and 291political wards. Four of its LGAs are urban, while the remaining 13 LGAs are mainly rural. The study was carried out in Aninri, Nkanu-east and Uzouwani LGAs representing the 3 senatorial zones of Enugu state, Nigeria. The 3 LGAs have a population of 236,221, 253,591and 227,150 respectively projected from 2006 census figures[42].

3.2 Study Population

Primary school pupil were recruited/ enrolled for this study for the following reasons (i) they are easy to access, (ii) the peak prevalence of schistosomiasis is known to be among this age group, (iii) experience has shown that there is generally good compliance from children and parents.[43,44]

3.3 Study Design

The study was a cross-sectional descriptive study in which urine samples were collected from primary school pupils both for parasitological and bacteriological analysis.

3.4 Sample Size Estimation

We adopted WHO recommendation that when a survey is organized to assess the need for control measures, 200-250 individuals should be an adequate sample for each ecologically homogeneous area in order to evaluate prevalence and intensity.[45] When research is conducted to evaluate parameters other than prevalence and intensity of infection (eg relationship with other diseases), a larger sample size will be required. We therefore had a pooled sample size of 900 for the study. This figure was divided among the 3 selected LGAs giving 300 for each LGA. This was in turn divided among the 3 selected schools and figure obtained divided among the 4 selected classes. All the pupils in each class who met the inclusion criteria were enrolled in each class.

3.5 Scope of study

The study covered only public primary school children in three randomly selected LGAs in Enugu state, Nigeria.

3.6 Inclusion/Exclusion Criteria

Primary school pupils who were below the age of 5 years and 15 years are excluded from this study. Females who had their last menstrual flow less than 24hours were also excluded

3.7 Sampling Method

A multi- stage sampling method was used. Enugu state has 3 senatorial zones. From each zone an LGA was randomly selected, among the rural LGAs in the area. Three primary schools were randomly selected from the list of public primary schools in each of the LGAs and four classes picked randomly in each school. Since our pooled sample size was 900, this figure was divided among the 3 selected LGAs giving 300 for each LGA. In each LGA, this was in turn divided among the 3 selected schools giving 100 pupils per school. The 100 pupils in each school obtained were divided among the 4 randomly selected classes in consideration of the state policy that public primary school classes should not have more than 30 pupils. All the pupils who met the inclusion criteria were enrolled in each selected class.

3.8 Data Collection

Disease Surveillance and Notification Officers (DSNO's) and focal persons were trained and used as interviewers.

Information on socio-economic, demographic, risk factors and clinical presentations was collected from every participant in the study using standardized questionnaires translated into a local dialect.

3.9 Lab methods

3.9.1 Sample Collection

A 20ml clean catch, mid-stream urine sample was collected in 50mls capacity autoclaved wide mouthed leak-proof universal containers by subjects themselves, who were previously carefully instructed with illustration aids. Samples were collected between 10.00am and 3.00pm which is the peak period for shedding of eggs. Each sample collected was divided into two fractions. About 10ml of each urine sample (fraction A) was investigated for the presence of S. haematobium *ova*. The remaining 10ml (fraction B) was investigated for bacteriuria. The specimens were appropriately labeled with identification numbers and placed in a cold box with ice packs, immediately after collection. Samples were immediately examined for visible haematuria and turbidity. The specimens were appropriately labeled with identification numbers and placed in a cold chain system with ice parks immediately after collection.

Laboratory analyses were carried out at Enugu State University of Science and Technology (ESUT) Teaching Hospital, Parklane, Enugu.

3.9.2 Laboratory Procedures

Fraction A was subjected to a commercially prepared reagent strip-Multistix 8 SG reagent strip (Siemens Lot 04200746) to check for the specific gravity, haematuria, leucocyturia, and proteinuria. This was dipped into each urine sample and the colour change was matched with standard colours by the side of the container of the reagent strips. For urine specific gravity values > 1.020 were considered significant[46]. Leucocyturia is considered significant >5 leucocyturic eosinophils/ hpf[47].

Thereafter this fraction was filtered through a 13-mm-diameter polycarbonate membrane with a 20um pore size. The filter was removed with forceps, placed on a glass slide and stained with a drop of 50% lugols iodine and examined under x40 light microscope and the number of eggs of S. haematobium eggs were counted and expressed as eggs / 10 ml of urine**.** Intensity was reported as the number of ova per 10mls of urine and categorized as light <50ova/10mls and heavy >50ova/10mls of urine.

Fraction B of all the samples that contained schistosome eggs were cultured on Blood agar and CLED agar plates respectively using the standard method[48]. All bacterial isolates thus obtained were characterized by using the standard methods[49]. Significant bacteriuria was described as bacteria count of equal or greater than 10^5 colony forming units per ml of urine (cfu/ml).

3.9.3 Quality Control

Quality control was undertaken to verify the consistency of the microscopic readings. Before the survey, a day was spent evaluating the consistency of egg counting among laboratory technicians by preparing 10 slides and comparing the reading of each slide by each laboratory technician with that of the team leader. A discrepancy of up to 5-10% for egg counts was taken as normal, but if the discrepancy was larger the reasons were identified and corrected. When one of the microscopists presented readings which are consistently different to those of the others in the team, he/she was excluded from the team. Each day during the survey, the team leader read 10% of the slides of each microscopist without prior knowledge of the result. In the case of a discrepancy larger than 10%, the slide was discussed by the two readers, and further slides examined to avoid repeated errors.

3.10 Data Analysis

To calculate the prevalence, descriptive analysis was done. Bivariate and multivariate logistic regression analysis was done to examine the association between some risk factors and schistosomiasis. Tables, proportions and percentages were used to summarize data obtained from the study. Graphs and charts were also employed for clarity of results. EPI-INFO version 3.5.1 and Microsoft Excel were used for data analysis.

3.11 Ethical Consideration

1. Approval was obtained from the ethical review committee of post graduate institute of medical research and training UNTH Enugu
2. We also got approval from the health/ education departments of the respective LGAs.
3. Oral informed consent was obtained from the Parents Teachers Associations (PTA) of the respective schools.
4. Participation by pupils was voluntary after obtaining assent. Information collected from participants was maintained with utmost confidentiality as names were not used on any sample but codes.

CHAPTER FOUR

RESULTS

A total of 842 primary school children out of a target of 900 participated in the study from the 3 LGAs selected giving a response rate of 93.6%. They were 262,309 and 271 from Aninri, Nkanu east and Uzouwani respectively. All were above the WHO recommendation of 200-250 for prevalence studies and gave a drop out of 4% and 0.7% for Aninri and Uzouwani respectively from the calculated sample size of 273 based on the 1989 prevalence of 79% in Amagunze[18]. The results are as presented below.

Table 1: Age group and gender distribution of respondents

Age group	Male(N/%)	Female(N/%)	Total(N/%)
5-8years	162(38.9)	136(31.9)	298(35.4)
9-12years	190(45.7)	246(57.8)	436(51.8)
13-15years	64(15.4)	44(10.3)	108(12.8)
Total	416(100)	426(100)	842(100)

The lowest age of respondent was 5years while the highest was 15years. The mean age was 11.4 years Std Dev 1.7. Median and modal ages were both 12 years. There was no significant difference in gender distribution among respondents as male /female ratio was almost 1 among respondents

Table 2: Prevalence of urinary schistosomiasis by age group and gender

Age-group	Male No(%) Infected	Female No(%) Infected	Total No(%) Infected	X^2
5-8yrs	43(26.5)	29(21.3)	72(24.2)	1.10
9-12yrs	71(37.4)	87(35.4)	158(36.2)	0.19
13-15yrs	40(62.5)	17(38.6)	57(52.8)	5.96*
Total	154(37.0)	133(31.2)	287(34.1)	3.15

*Significant

The table shows a pooled prevalence of 34.1%. The highest prevalence of urinary schistosomiasis (52.8%) was among age-group 13-15years even though the group presented the least number of participants. Most of the pupils infected were above the age of 8years. Infection rate was higher in males154/416(37%) than females 133/426(31.2%) but not statistically significant(X^2=3.15).

Table 3: Prevalence of urinary schistosomiasis by schools

Parameter	No examined	Total No(%) Infected
Aninri		
PS Ezza-ndeaboh (A)	85	33(38.8)
PS Ezza-mpu(B)	87	27(31.0)
Central Sch Mpu©	90	35(38.9)
Total	262	**95(36.3)**
Nkanu east		
Riverside PS(D)	103	68(66.0)
CPS Isienu(E)	101	37(36.6)
CPS Aniyi(F)	105	28(26.7)
Total	309	133(43.0)
Uzouwani		
Cent Sch Adani(G)	91	22(24.2)
UPS, Opanda(H)	88	28(31.8)
CPS, Opanda(I)	92	7(7.6)
Total	271	59(21.8)
Grand total	**842**	**287(34.1)**

Table 1 presents the prevalence rate of *S. haematobium* infection in the three LGAs of Aninri, Nkanu-east and Uzouwani respectively. Infection rate was higher in Nkanu east133/309(43.0%) than Aninri 95/262(36.3%) and Uzouwani 59/271(21.8%).The highest prevalence of 66% was among respondents from Riverside primary school in Nkanu east LGA while the least (7.6%) was in Community primary school, Opanda, Uzouwani LGA.

Table 4: Classification of infection by intensity

Parameter		Male		Female		Total	
		light	heavy	Light	heavy		
Age group		infec	infec	infec	infec	Light infec	heavy infec
5-8 years	31	12	8	21		39	33
9-12years	26	45	23	64		49	109
13-15years	15	25	4	13		19	38
Total	72	82	35	98		107(37.3%)	180(62.7%)

High intensity/heavy infection (eggs > 50/10mls of urine) accounted for over 62% of cases. Intensity ranged from 21 to 1138eggs/10mls of urine. Mean egg count was 348/10mls urine(# 178.1) The percentage heavy intensity was significantly higher in females than males (X^2=12.8) and 9-12year age group(X^2=5.9) than other age groups.

Table 5: Validity of some morbidity markers

Positive N=287, Negative N=555

Marker	Positive infected	Negative /uninfected	Sensitivity	Specificity	PPV	NPV
Haematuria	237	31	83	94	88	91
Proteinuria	209	92	73	83	69	86
Turbidity	127	59	44	89	68	76
sp.gravity	134	47	47	92	74	77
Leucocyturia	281	115	98	79	71	99

The table shows that leucocyturia presented the highest sensitivity and NPV while haematuria presented the highest specificity and positive predictive value.

Table 6: Prevalence of bacteriuria among schistosomiasis cases by sex in the three LGAs

LGA	Male N=416				Female N=426			χ^2
	ova	ova with uti/%	uti no ova	X2	ova	ova with uti/%	ova no uti	
Aninri	44	29(65.9)	5	47.7	51	16(31.4)	4	19.9
Nkanu east	73	36(49.3)	2	43.8	60	39(65.0)	5	66.5
Uzouwani	37	19(51.4)	2	55	22	15(68.2)	2	67.7
Total	154	84(54.6)	9	146	133	70(52.6)	11	141.9

This table shows prevalence of concomitant urinary tract infection among male and females with urinary schistosomiasis to be 54.6% and 52.6% respectively,(X2=0.11). The combined prevalence was 53.7% in those infected and 3.6% in uninfected. Generally the presence of ova in urine was found to be a significant risk factor for bacteriuria among school age children(X2=141.9).

Table 7: urinary tract pathogens secondary to urinary schistosomiasis by gender

Bacteria Agent	Male (N=84) No positive(%)	Female (N = 70) No positive(%)	Total (N=287) No positive(%)	X^2
Klebsiella Species	25(29.8)	20(28.6)	45(29.2)	0.03
Eschericha coli	43(51.2)	32(45.7)	75(48.7)	0.46
Staphylococus aureus	12(14.3)	10(14.3)	22(14.3)	0.00
Proteus Species	2(2.4)	2(2.9)	4(2.6)	P(0.62)
Pseudomonas species	2(2.4)	6(7.1)	8(5.2)	P(0.09)
TOTAL	84(100)	70(100)	154(100)	

The table shows that the predominant urinary pathogens associated with urinary schistosomiasis were Escherichia coli, Staphylococcus aureus, and Klebsiella Species. It is pertinent to observe that there was no significant predilection of any of the isolated organisms to any particular gender as shown by the test of significance.

Table 8:Association between some exposure factors and urinary schistosomiasis in Enugu state, Nigeria; July 2011

Variable(exposure factor)	Infectcted n=287(%)	uninfected n=555(%)	Odds ratio 95%CI
Parents occupation(farming)	227(79.1)	428(77.1)	1.12(0.78-1.61)
Sex(male)	154(53.7)	262(47.2)	1.29(0.96-1.74)
Distance of household from water body(<1km)	92(32.10)	32(5.8)	5.74(3.59-9.21)*
Frequent visits to water bodies (daily& more)	244(85.0)	250(45.1)	6.92(4.74-10.14)*
Type of toilet facility (bush system)	69(24.0)	123(22.2)	1.11(0.78-1.58)
Main source of water to the family(stream)	266(92.7)	291(52.4)	11.49(7.00-19.03)*
Age >13 years	57(19.9)	51(9.2)	2.45(1.60-3.38)*
Family size(>4)	253(88.2)	484(87.2)	1.09(0.69-1.73)

* Significant

The table shows that there is significant association between urinary schistosomiasis and the following: the distance from the open water body, frequent visits to water bodies, source of water to the household and age. Other factor such as gender, type of toilet facility are not found to have significant association

CHAPTER FIVE

DISCUSSION

This study was carried out to determine the current prevalence of urinary schistosomiasis, factors associated with infection and the prevalence of concomitant bacteriuria in Enugu state. This is important since the only study carried out was in 1989[18]. Moreover the last mass drug administration (MDA) in the state was in a distant past in 1998. The socio-demographic data showed that children above 13 years accounted for 12.8 % of the respondents. The high number of children in this age bracket who were still in primary school points to delayed schooling which presently could be attributed to schistosomiasis infection[6]. The high number of respondents rather than rejection from Nkanu east known to be endemic shows the level of awareness about the disease in the area. This might signify that they see it as their problem and are begging for solution. Similarly the good response rate as depicted by low drop-out rate also gives credence to the general belief that children give better compliance.[43,44]

The study also showed a pooled prevalence of 34.1% of urinary schistosomiasis among the school age children in the three randomly selected LGAs. This result is in contrast with 79% in Amagunze, Nkanu east LGA of the state[18]and 79.4% in nearby Ezza North LGA of Ebonyi state lying in the same geographical zone of Nigeria[50]. The differences in prevalence among these studies could be attributed to reduction in water contact practices due the availability of some borehole in the areas as well as residual awareness created during the periods of mass drug administration (MDAs).On the other hand, the difference in the prevalence obtained from previous studies could be attributed to the different diagnostic technique used for schistosomiasis; the sedimentation methods used in the two referenced studies is more sensitive than the syringe filtration technique used in the present study. Also there could have been an underestimation since only one urine sample/subject was examined as against WHO recommendation of multiple samples especially in light infections. When the prevalence is stratified according to LGAs, Nkanu east has the highest prevalence of 43% as against 36% and 21% for Aninri and Uzouwani LGAs. Moreover, the school that recorded the highest prevalence and intensity was also in Nkanu east LGA. This is not surprising as the previous studies had shown that the disease is endemic around the area.[18] However, all the figures were above the Nigerian national mean of 13%[56] (Oforeze 2002). There was no significant difference in the prevalence between males (37.0%) and females (31.2%) x^2= 3.15. This may be an indication that both gender and all ages are being equally exposed to infection through water contacts as there is no cultural barrier against any gender or group. The fact that both genders had similar prevalence agrees with previous reports that *S. haematobium* infection is not gender-specific in many parts of Nigeria.[51,52] There was significant difference in the infection rate among the age groups with 13-15years recording the highest prevalence of 52.8%.This is similar to findings in other studies elsewhere,[57] This could be explained by the fact that children are more adventurous around this age and therefore more likely to have more contact with water bodies. and disagrees with findings in Ogun state that the peak of infection was at 8-10 years[58] In Enugu state, the risk of schistosomiasis infection is wide spread as evidenced by the prevalence in all the surveyed LGAs

In our study, heavy intensity accounted for 62.7% of positive cases of urinary schistosomiasis. This is comparable to 74.4% in Ikpeshi LGA, 59.5% in Ogben, Owan East LGA both of Edo state[53-54] and Ezza north of Ebonyi state[50] . Observed similarity might be linked to all being in the same ecological zone that is probably favourable to the snail intermediate host for transmission. It differs from the findings in a similar rural community in Malawi where heavy intensity was found to be 2.4%.[55] The difference might be attributed to differences in ecological zones and probably the effectiveness of the intervention programmes in Malawi. More females than males had heavy intensity(X^2=12.8). IT is known that in the part of the world, young girls do most the domestic activities which include fetching water for general domestic uses, going to streams for laundry etc. They therefore are more exposed to water bodies than their male counterparts. The percentage heavy intensity was also significantly observed to be higher among th9-12 year age group(X^2=5.9). The higher rate of heavy intensity at this age group may be due to high water contact activities in the phase of low immunity. Immunity is said to develop with age and exposure. At this age, children have not fully developed immunity and have increasing adventurous tendencies leading them to frequent water contacts and hence more exposure with low immunity.

The use of some morbidity markers to assist in community diagnosis has been emphasized by many authors. Proteinuria and haematuria reported in this present study had been documented in earlier reports[1234567]. The sensitivities of these two markers as well as that of specific gravity and turbidity were found to be high. High prevalence of these markers may be a reflection of the level of renal involvement and morbidities, which may also need further investigations. It is also an indication of predisposition of these school age children to renal complications associated with urinary schistosomiasis. The evaluation of these parameters as diagnostic index for schistosomiasis appears scanty.

We reported a sensitivity, specificity, positive predictive and negative predictive value of 83%,94%,88% and 91% respectively for haematuria as a diagnostic marker. This is similar to the findings in Malawi for haematuria with sensitivity, specificity, and NPV of 68.3%, 73.6%and 95% respectively[55]. However, the PPV of 91% was obtained as against 23.3% in Malawi. This may be due to the type of strip which potency may vary according to environmental changes. The sensitivities of the markers in our report also compare with the result of a study in Edo state[8] with Haematuria 80%, Proteinuria 56%, Specific Gravity (SG) 84%, Turbidity 76%, Eosinophilia 100%

Of the 287 pupils with ova/egg in urine, 154 (53.7%) had bacteriuria while those not infected had 3.6% UTI prevalence. Therefore, the presence of schistosoma haematobium ova was generally significantly associated with the prevalence of bacteriuria(X^2=141.9). This result is comparable to the findings in Ngbo west (48.3%}- a similar rural community in the same socio-cultural and ecological zone with known high prevalence of urinary schistosomisis.[50] The different prevalence in the infected and uninfected is also similar to findings in a survey of school children in Egypt(Laughlin) This high rate of concomitant bacteria urinary tract infection in children where ordinarily UTI is known to be low could be attributed to urinary schistosomiasis. During infestation, as schistosoma haematobium eggs are being ejected into the urine, some blood also leaves with the eggs concurrently from the bladder. Blood being a potential culturing medium can encourage the onset of bacteria urinary tract infection. This is known to be documented as potential risk factor in the incidence of squamous cancer of the bladder in later years as studies have shown in some countries.[7,8,34-36] However we did not check for other possible factors that predispose to urinary tract infections in children in rural communities such as poor sanitary habits. Our study did not show any significant difference in the prevalence between the males 54.6% and females 52.6% (x^2=0.11). UTI is known to have no sex preference at this age range(5-15years).

The most common organisms isolated in the study are E. coli, Klebsiella and staphylococcus auerus. This is similar to the findings by in some other states in Nigeria such as Ebonyi[50] and

Edo states.[54] No significant difference was observed in the prevalence of these organisms between males and females. This is basically due to the fact that virtually all the infections can be said to be secondary to urinary schistosomiasis and both sexes were affected.

Closeness to water bodies (OR= 5.74(3.59-9.21)) and frequent visits to water bodies at least once daily(OR=6.92(4.74-10.14)) were found to be the two major factors predisposing children to the risk of urinary schistosomiasis. This agrees with the findings in a study in south western, Nigeria in 2010.[57] It goes to show that by controlling the frequent visits to the stream, the risk of urinary schistosomiasis could be reduced.

Limitations of the study:

It was not easy to collect information from children. We did not study the non enrolled school age children as well as pre-school children. Samples of snails were not taken to ensure the infections were not imported. We also did not carry out antibiogram to determine the sensitivity of the organisms isolated.

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CHAPTER SIX

CONCLUSION/RECOMMENDATIONS

The study has been able to establish the current prevalence and intensity of urinary schistosomiasis in Enugu state. It showed that there is moderate prevalence of schistosomiasis in Enugu state being facilitated by frequent visits to water bodies and closeness of water bodies to the people at risk of infection. This places the area in category 2 (20-50% prevalence) and qualifies them for targeted mass drug administration according to WHO guidelines.The study also showed that a combination of haematuria and proteinuria still remains relevant for community diagnosis of urinary schistosomiasis as shown by their sensitivity, specificity and positive predictive values A high level of associated bacteria urinary tract infection in those infected with urinary schistosomiasi was established. The import of this is that since the co-infection with bacteria has been implicated in the aetiology of bladder cancer due to release of amines, the state stands a risk of experiencing high incidence of bladder cancer in the near future if nothing is done

. In the light of the above we wish to recommend that:

(1) intensive health education should be carried out to sensitize the people on the risk of frequent visits to water bodies by children, urinating around water bodies as this will help in spreading the infection, and other measures to prevent infection. This could be done through community dialogue.

(2) Efforts should also be made to treat people identified to be infected using WHO guidelines as they would continue to spread the disease through common water contamination.

(3) In order to prevent complications in infected individuals, control programme should incorporate the co -administration of antibiotics to take care of these bacteria co-infection. By so doing many of the complications could be averted.

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Appendix I

URINARY BACTERIA INFECTION ASSOCIATED WITH URINARY SCHISTOSOMIASIS AMONG SCHOOL AGE CHILDREN IN RURAL COMMUNITIES IN ENUGU STATE, NIGERIA.

SAMPLE QUESTIONNAIRE

Questionnaire No:

Unique Identification No: ..... Date: ...……

Name of school/community------------------ LGA-------------------

Height---------------------- Weight---------------------------

SECTION A: DEMOGRAPHIC DATA

1. Age in years: (a) 5 – 8years ( ) (b) 9-12 years ( ) (c) 13-15 years ( )

2. Sex: (a) Male ( ) (b) Female ( )

3. Religion: (a) Christianity ( ) (b) Islam ( ) (c) Traditional ( ) (d) Others ( )

4. What level/ class are you in school? (a) Primary 1-3( ) (b) primary 4-6( )

5. How long have you lived in this community in years? --------------------------

SECTION B: SOCIO-ECONOMIC FACTORS (TICK AS APPLICABLE)

5. Father's occupation: (a) unemployed ( ) (b) farming ( ) (c) trading ( ) (d) civil servant ( ) (e) artisan ( ) (f) others ( )

6. Mother's occupation: (a) unemployed ( ) (b) farming ( ) (c) trading ( ) (d) civil servant ( ) (e) artisan ( ) (f) others ( )

7. Highest educational level attained by father: (a) None ( ) (b) primary ( )

(c) junior secondary ( )(d) senior secondary ( ) (e) tertiary ( )

8. Highest educational level attained by mother: (a) None ( ) (b) primary ( ) (c) junior secondary ( ) (d) senior secondary ( ) (e) tertiary ( )

9. How many are you in the family(family size)------------------------

10. Which type of toilet facility do you use in your family?

(a) Bucket system ( ) (b) bush system ( ) (c) pit latrine ( ) (d) VIP toilet ( )

11. What is your source of water in the family?

(a) Well ( ) (b) stream/pond/river/lake ( ) (c) pipe borne water ( )

12. What is your source of water in the school?

(a) Well ( ) (b) stream/pond/ river/ /lake ( ) (c) pipe borne water ( )

Section C: Risk factors (tick as appropriate)

13. Are there water bodies eg pond, stream, lake or river, dam around your home?

Yes ( ) No ( )

14. What is the estimated distance of the water bodies from your house?

(a) Less than 1 kilometer ( ) (b) 1-5 kilometers ( ) (c) greater than 5 kilometers ( )

15. If yes do you go to the water body to bath/swim?

Yes ( ) No ( )

16. Do you go to the stream to wash cloths?

Yes ( ) No ( )

17. Do you go to stream to fetch water for domestic use?

Yes ( ) No ( )

18. If yes to any of the above, how often

(a) Daily ( ) (b) weekly ( ) (c) monthly ( )

19. Are there snails around the water bodies?

Yes ( ) No ( )

20. Do you have any water bodies eg pond, lake or river, dam around your school?

Yes (   )   No (   )

21. What is the estimated distance from your school?

(a) Less than 1 kilometer (   ) (b) 1-5 kilometers (   ) (c) greater than 5kilometers (   )

22. Do you play or bath in this open water?

(a) Yes (   )   (b) No (   )

23. If yes, how often?

(a) Daily or more (   )   (b) weekly (   )   (c) monthly (   )   (d) yearly (rarely)   ( )

24. Are there snails around the water bodies?

Yes   (   )   No (   )

Section D: Clinical symptoms and signs (tick as appropriate)

25. Have you been passing blood in urine in the last one month?
Yes (   )   No (   )
26. Have you been urinating frequently more than 6times/day) in the last one month?
Yes (   ) No (   )
27. Did you have pain while urinating   Yes (   )   No (   )
28. Did you have lower abdominal pain   Yes (   )   No (   )
29. Others   please specify……