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Evaluation of the health impact of integrated helminths control by preventive chemotherapy in the selected endemic districts of Tanzania.

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I hereby confirm that the submitted version of the revised dissertation contains the required necessary improvements in a sufficient degree.

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Evaluation of the Impact of Integrated Helminths Control by Preventive Chemotherapy in selected Endemic Districts of Tanzania.

Key Words

Schistosomiasis, hookworm, prevalence, anaemia, stunting, underweight, helminth infections

Abstract

Neglected helminths affect nearly a billion people in developing countries. This study aimed to investigate: 1) impact of preventive chemotherapy (PCT) on helminth infections; 2) polyparasitism and associated health indicators; 3) associations of helminth infections and atopy.

The study was undertaken in rural and urban districts of Tanzania. The rural districts were Kwimba and Sengerema (Mwanza region and the urban districts were Kinondoni and Temeke (Dar es Salaam region). A total of 2,708 and 2,431 study participants were enrolled in the surveys conducted from June to July in 2013 and June to October in 2014 respectively. In 2013, one round of treatment with ivermectin and albendazole was administered to the whole population 5 years and above and praziquantel administered to School aged children (SAC) in Dar es Salaam districts. In Mwanza districts, albendazole and praziquantel were administered to SAC. Study participants included at total of school children 1,391 in the year 2013 and 1,084 in the year 2014 who were aged 5-17 years. Urine, stool samples and anthropometric measures were taken from 5-17 years old while blood samples were taken from all participants. Laboratory tests included: stool microscopy for soil transmitted helminths (STH) and *Schistosoma mansoni*; urine microscopy for *Schistosoma haematobium*; and blood tests for lymphatic filariasis, malaria and full blood count. Children aged 5-17 years underwent skin prick test with dust mite and cockroach allergens.

In 2013, the overall prevalence of lymphatic filariasis (LF) was 45/2,681 (1.7%) *S. haematobium* was 73/749 (9.8%) *S. mansoni* 11/752 (1.5%) and hookworm infection was 21/752 (2.8%).The Geometric Mean Intensity (GMI) for *S. haematobium* was 10.4 egg/10ml among infected participants while the intensity of *S. mansoni* and hookworm were 410.8 and 318 eggs per gram of stool (EPG) among infected participants respectively.

In 2014, prevalence of *S. haematobium* was 22/804 (2.7%), 11/752 (1.4%) for *S. mansoni,* 17/804 (2.1%) for hookworm and 37/2,321 (1.6%) for LF. The GMI for *S. haematobium* was 7.8 egg/10ml of urine among infected individuals while the GMI for *S. mansoni* and Hookworm were 40.4 and 70.7 EPG respectively.

In both years of surveys, no cases infected with *Trichuris trichiura* or *Ascaris lumbr*icoides were found. Moreover, none of the cases infected with *Schistosoma species* were noted in urban areas. LF was found more in urban and rural areas.

A crude reduction in prevalence of *S. haematobium* by 74% (p<0.001) in 2014 compared to 2013 and also 67% for *S.mansoni* infection (p=0.052). There was no significant change in prevalence of hookworm and LF infections. Furthermore, a significant reduction of GMI of *S. mansoni* and hookworm was observed.

Univariate associations were observed between stunting and *S.mansoni* (p=0.06) and hookworm (p=0.002) while for anaemia was between *S.haematobium* (p=0.01), hookworm (0.002) and malaria (p<0.001). Multivariate associations of infection and health indicators included: hookworm with stunting (p=0.03) anaemia with and anaemia with malaria (p<0.001).

After one round of PCT about 38% reduction in overall stunting was noted but was not significant in participants infected with helminth infections. Anaemia decreased in urban areas by 47% after one round of MDA while it generally increased mostly in rural areas despite an effective treatment of helminth infections. This increase is explained by an increased prevalence of malaria which was also noted.

Univariate association indicated that participants from rural areas were more often positive for the skin prick test using *Dermatophagoides farinae* (p=0.0001) and *D. pteronyssinus* (p=0.004) allergens and for cockroach was less by 60% (p=0.0004). Hookworm infection was associated with reaction to *D. pteronyssinus* (p=0.01) and *S.mansoni* infection was associated with D.farinae (p=0.06). In multivariate analysis, only hookworm and *D. pteronyssinus* dust mite were significantly associated (p=0.005).The reasons for these findings need to be addressed in further studies. However, one explanation would be cross reactivity of allergens with helminths antigens.

A reduction in prevalence of *S. haematobium* and intensity of *S. mansoni*, and hookworm was observed following one round of MDA. Moreover, a positive association between helminth infections prevalence and its impact indicators was observed. Therefore, multiple MDA and longitudinal monitoring of infection and health indicators is recommended.

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List of abbreviation

AIC-Akaike Information criterion

ALB-Albendazole tablet

APOC-African Programme for Onchocerciasis Control

CCHP-Councils Comprehensive Health Plans

CDC-Center for Disease Control

CDTI-Community Directed Treatment with Ivermectin

CFA-Circulating Filarial Antigen

CI-Confidence Interval

CIH-Center for International Health

Cm-centimeters

DEC-Diethylcarbamizine

EDTA- Ethylenediaminetetraacetic acid

ELISA-Enzyme Linked Immunosorbent Assay

FGD-Focused Group Discussions

GMI-Geometric Mean Intensity

GNNTD-Global Network for Neglected Tropical diseases

GPELF-Global Program to Eliminate Lymphatic Filariasis

GPELF-Global Programme for Elimination of Lymphatic Filariasis

GPS-Geographical Positioning System

GSK-Glaxosmithkline

GTZ- Deutsche Gesellschaft für Technische Zusammenarbeit GmbH *(German: German Agency for Technical Cooperation)*

Hb-haemoglobin level

ICT-Immunochromatographic Test

IEC-Information Education and Communication

IVM-Ivermectin tablets

KAP-Knowledge Attitude and Perceptions

Kg-Kilogrammes

LF-Lymphatic Filariasis

LLINs-Long Lasting Insecticidal nets

LMU-Ludwig Maximilians Universitat

MDA-Mass Drug Administration

MEB-Mebendazole

MEC-Mectizan (ivermectin) tablet

Mf-Microfilaria

Mg-milligrammes

Ml-milliliters

MOH-Ministry of Heath

MRCC-Medical Research Coordinating Committee

MUAC-Mid Upper Arm Circumference

NIMR-National Institute for Medical Research

NIMR-National Institute for Medical research

NLEFP-National Lymphatic Filariasis Elimination Program

NTD-Neglected Tropical Diseases

OCP-Onchocerciasis Control Programme

ODK-Open Data Kit

PCR-Polymerized Chain Reaction

PCT-Preventive Chemotherapy

PPS-Probability Proportional to Size

PZQ-Praziquantel

RECTID-Research Center for Tropical Infectious Diseases

SAC-School Aged Children

SCH-Schistosomiasis

STH-Soil Transmitted Helminthiasis

THMIS-Tanzania HIV and Malaria Indicator Survey

WBC-White Blood Cells

WHA-World Health Assembly

WHO-World Health Organization

1. INTRODUCTION

1.1. Overview and organization of the thesis

This study was conducted with the overall goal to determine the impact of Preventive Chemotherapy (PCT) also known as Mass Drug Administration (MDA) on helminth infections in rural and urban endemic districts of Tanzania. The work was done in year 2013 and 2014 in selected 4 districts 2 in Dar es Salaam regions (urban) and 2 in Mwanza (rural) districts. This thesis work is designed to describe the global and regional burden of helminths specifically together with its correlation with health indicators such as anaemia and nutritional status. A description of the control and elimination efforts at global and regional level is also included. The situation of helminth infections burden and control efforts in Tanzania is also described in detail.

The rationale of the study is stipulated to describe the gap in understanding the effect of MDA on helminth infections and its associated heath indictors in endemic communities. Description of the Study design, approach used to collect data and analysis is provided in the methods and procedures sections. Included in the results section is the study population, prevalence of helminth infections, intensity of helminth infections and association between health indicators and helminth infections. Furthermore the relationship between helminths and allergies specifically against house dust mites (*Dermatophagoides farinae, D. pteronyssinus*) and cockroach (*Blatella germanica*) was also described. The discussion section explains in detail the study findings and its comparison to what other researchers have found in same aspects in various settings of the world.

1.2. Neglected tropical diseases and helminth infections

Neglected Tropical Diseases (NTDs) are a group of chronic diseases that are endemic in tropical and subtropical countries. NTDs persist in the poorest and the most marginalized communities in rural and urban places with unsafe water, poor sanitation, and limited access to basic health care [1, 2]. Neglected Tropical Diseases can be fatal, but primarily cause acute clinical symptoms and chronic lifelong disabilities, leading to disfigurement, impaired child growth, poor pregnancy outcomes and impaired economic development [3].

The World Health Organization (WHO) estimates that at least one (1) billion people are affected from one or more of the NTDs. A further two(2) billion are at risk of infection in tropical and subtropical countries [4]. NTDs are associated with poverty and various disadvantages. It is estimated that 1.2 billion of the world's poorest (2.7 billion living on less than US$2 per day) are affected by NTDs [5].

NTDs are caused by helminths, bacteria, viruses and protozoa and almost exclusively affect impoverished people living in rural areas or urban slums in low income countries[6]. In Sub-Saharan Africa, almost 85% of the burden of NTDs is due to helminths [7, 8].

Recognizing the public health and socio-economic consequences associated with NTDs; particularly those caused by helminths namely- Lymphatic Filariasis (LF) Onchocerciasis and Soil Transmitted Helminthiases (STH); the WHO and other partners rose to the challenge and spearheaded efforts for the control of NTDs. In December 2003, the WHO, the Germany Technical Cooperation (GTZ) the German Ministry of Development and Technical Cooperation (KFW) the German Ministry for Health and Social Security and the Special Programme for Research and Training in Tropical Diseases (TDR) hosted the first WHO/GTZ meeting involving experts from various sectors. The meeting set the agenda for intensified control of NTDs as a group (due to diseases overlap) rather than a disease specific approach. Another meeting was held in April 2005 in Berlin after which an NTD department was formed at the WHO. A partners meeting on NTDs was held in April 2007 bringing together partners from endemic countries, pharmaceutical and donor countries to gain support for NTDs. From this time an integrated diseases centered approach to health needs for quick wins and meeting the MDGs targets was realized. Moreover, multiple approach including strengthening vector control, broader rapid coverage of interventions, improved surveillance and care for affected populations has been attained. WHO headquarters through its NTD department works in a cascade manner, where by its regional offices are located in all continents. Regional offices work with WHO-country offices. In Sub-Saharan Africa the office responsible for NTDs is known as WHO AFRO. At WHO – AFRO, NTDs are under the communicable Diseases cluster. Currently, there is a special project for the elimination of NTDs (ESPEN) which coordinates the control and elimination of the 5 PCT diseases namely; LF, Trachoma, STH, Onchocerciasis and Schistosomiasis.

WHO headquarters has been working through its regional and country offices in collaboration with multiple stakeholders, including ministries of health in endemic countries .Endemic countries have adopted various WHA diseases specific resolutions and have stepped up efforts to eliminate these diseases from endemic districts/areas. Majority of endemic countries have initiated the control and elimination programmes, whereby donated medicines are distributed through MDA. The free donations of Medicines is done by Pharmaceutical companies such as Pfizer, GlaxoSmithKline (GSK) and Merck.

These efforts on NTD elimination and control were reinforced in 2012 when the London Declaration on NTDs came into effect/or was initiated. Through the declaration donors and endemic country governments, private sector leaders, pharmaceutical companies and multilateral organizations made commitments and announcements for a close partnership to control or eliminate NTDs by 2020, in line with World Health Organization (WHO) targets and the 2020 Roadmap on NTDs [9]. In 2013 a comprehensive resolutions WHA66.12 was adopted which calls for member stated to implement, expand and monitor NTD control and elimination activities[10].

1.3. Background

1.3.1. Neglected Helminth infections: the global situation and Preventive Chemotherapy (PCT)

Among NTDs, helminths are estimated to be spread worldwide, especially in the tropics and sub-tropics. Africa accounts for about 85% of disease burden due to helminths [7]. Among the NTDs; there are 4 helminthic diseases that are targeted for preventive chemotherapy through MDA: soil-transmitted helminthiases, schistosomiasis, lymphatic filariasis (LF) and onchocerciasis [6, 8].

Preventive chemotherapy is the strategy recommended by WHO to alleviate the suffering, reduce morbidity and interrupt transmission of helminth infection using quality medicines. The intervention is administered at population level at regular intervals for a defined period of time. PCT, sometime referred to as Mass Drug Administration (MDA) involves treatment of entire endemic population regardless of individuals' infection status. PCT has shown to have significant impact on helminth health indicators such as its prevalence and intensity, relationship with nutritional status (stunting, underweight and wasting) anaemia as well as lesions of urinary tract and liver [11, 12]. Several

studies have indicated a reduction of disease prevalence and intensity following MDA with anthelminthic medicines. For instance, Zhang *et al*., found a significant reduction of prevalence and intensity of infection with helminth in high risk population in Uganda after only 2 years of treatment [13]. In Burkina Faso, it was revealed, that even a single round of mass chemotherapy could have a substantial impact on *S. haematobium* infection and its associated morbidity in children [14].

Anaemia is acknowledged as one of the most important public health concerns world-wide with estimates from WHO showing two billion people to be affected [15]. Multiple factors are reported to be the causes for anaemia. However, anaemia due to iron deficiency is largely caused by parasitic infections including helminths. Helminths such as STH cause anaemia mostly in children and pregnant women. Studies in Uganda and Tanzania have revealed that anaemia associated with schistosomiasis and geohelminths like hookworm can be significantly reversed with chemotherapy [16, 17]. Furthermore studies indicate that coexistence of multiple helminth infection have an effect on anemia despite the low intensity profile [18].

1.3.2. Helminths and eosinophilia

The eosinophils are white blood cells responsible for inflammatory processes including allergic disorders. Eosinophilia is a condition in which blood cells known as eosinophils count is greater than 7% of the circulating white blood cells (WBC) [19]. It is known to be caused by several factors including atopy, parasitic infections like helminthes and neoplastic disorders. Correlation of helminth infections and eosinophilia has been studied in various places. Most results indicate that eosinophilia can serve as one of the clues for helminths infections if other causes are excluded [20-22]. *Leder et al.* found that multiple helminth infection is associated with eosinophilia [23]. Furthermore, a study conducted in southern Spain on immigrants indicated that eosinophilia was resolved in 93.9% individuals after empirical treatment with albendazole, ivermectin and praziquantel [24].

1.3.3. Helminths and atopic diseases

Atopy, sometimes used interchangeably with allergy, refers to an inherited tendency to produce IgE antibodies in response to small amounts of common environmental proteins such as pollens, house dust mites and food allergens. Most commonly atopy affects the nose, eyes, skin and lungs. Atopic disorders include extrinsic atopic dermatitis, immune-mediated urticaria, immune-mediated

angioedema, some allergic lung disorders, like asthmatic diseases (allergic Asthma) and allergic venomous stings.

Allergic diseases are becoming an important health threat both to individuals and society because they have reached epidemic proportions in developed and developing countries as well [25]. Atopic diseases are more common among adolescents beginning from childhood. They manifest firstly, as atopic dermatitis which is considered an initial stage in the atopic march. It is a very common inflammatory skin condition which poses a considerable cost on the health care system. It affects 15%-20% of children and 1-3% of adults' worldwide [26].

Relationship between helminths and allergic diseases has been reported in several studies. Decades ago an increase in allergic diseases and asthma was noted in industrialized countries Efforts were undertaken to control infectious diseases and the so called "hygiene-hypothesis" was formulated by D. Strachan [27, 28]. A negative association was described between different helminth infections [29, 30]. Although helminthes can modulate the host inflammatory response directed against the parasite, a causal association between helminthes and atopic diseases remain uncertain. Different helminth parasites may have different effects on allergy depending on the time of exposure[31]. To date, reports on the relationship between the infections with helminthiases and allergies have been contradictory [32-34]. There are findings that have indicated helminthes infection have negative association with allergies [35, 36] while other have shown a positive association [37]. Helminth eradication programmes are challenged with the question of whether their efforts may lead to an increase in atopic diseases. However, a randomized study done in Ecuador indicated that there were no increased atopic symptoms between the group that received two monthly albendazole and the one that did not receive albendazole [38]. Although several studies have been done in the area of multiple infections, interrelationships between helminth infections and atopic diseases, the ongoing discussion and inconclusive results require more studies.

1.3.4. Helminth existence in urban and rural areas

The existence of helminth infections has been studied extensively in both rural and urban areas. The difference in prevalence depends on cultural, occupational, social and environmental factors. A study by Curtale *et al*., in Egypt indicated that urbanization has deteriorated the living conditions

and sanitation thus attracting helminth infections [39]. A study in Pemba Island indicated no difference in intestinal infections among rural and urban children [40].

1.3.5. Helminth and Nutrition

Helminth infections have effect on nutritional status due to the fact they feed on blood and other gut contents of host individuals. This brings about loss of appetite as well as impaired growth and development of host individuals Nutrition status indicators includes stunting, thinness and underweight. Numerous studies indicate the co-prevalence of nutritional disorders and STH infections in developing countries. Studies conducted in Ghana, Tanzania, Vietnam, India and Indonesia showed that the prevalence of stunting ranged between 48% and 56% while that of underweight ranged between 34% and 62.% [41].Moreover, the World Development Report (2011) indicated an estimated 100 million people have experienced stunting or wasting as a result of geohelminths infections[42].

On the other hand, interventions to eliminate helminth infections have as one of their aims been to reduce problems associated with nutrition status (WHO, 2001). In Uganda for instance, studies indicated weight gain of 10% above the expected among school children in areas where periodic provision of anti-helminthic treatment was conducted [43].

1.4. Epidemiology of Neglected Helminth infections

1.4.1. Schistosomiasis

Schistosomiasis is one of the most common helminth infections, endemic in 76 countries with 652 million people at risk of infection [44]. It is estimated that 203 million people are infected with schistosomiasis worldwide, with more than 90% of the disease burden in sub-Saharan Africa [45]. Schistosomiasis is caused by infection with trematodes *S. mansoni, S. mekongi, S. japonicum* and *S. intercalatum.* Urinary Schistosomiasis is caused by infection with *S. haematobium*. The major contributory factors to such high levels of infection are limited access to safe water and lack of or poor environmental sanitation. Individuals are therefore continually exposed to the parasites and re-infection levels are high (in most areas). The consequences of these diseases include blood in urine, diarrhoea, hepatomegaly (35%) and/or splenomegaly (80%) [46]. Chronic intestinal

schistosomiasis results in severe organ pathology such as hepatosplenomegaly, periportal liver fibrosis and portal hypertension which progress from abdominal pain and bloody diarrhea. Urogenital schistosomiasis leads to hematuria, dysuria, hydronephrosis and calcification of the bladder and seem to increase the risk of those with HIV infection [47]. These morbidities contribute to, amongst others, anaemia, growth stunting and cognitive impairment in infected individuals [17, 48]. Globally, schistosomiasis alone is estimated to cause about 300,000 deaths per year, although this is thought to be a significant underestimate because the schistosomiasis-related deaths are rarely stated as such in hospital records and death certificates [48].

Control of Schistosomiasis aims to reduce transmission of parasites and reduce the level of infection in individuals in order to minimize the pathological effects. The predominant intervention for control is annual treatment with one dose of praziquantel (PZQ, at 40mg/kg) where number of tablets received is determined by a dose pole which: devised as proxy for weight to be used in MDA settings [51]. Annual treatment should be supported by improved access to safe water, adequate sanitation and where feasible, snail control [45, 49]. Mass chemotherapy campaigns with PZQ are targeted at school-age children (SAC) as they harbor the heaviest worm burden in a population. The target should be to reach at least 75% therapeutic coverage of SAC at risk of infection [53]. WHO also recommends that those at high-risk, for example, fishermen and women who frequently visit contaminated water sources, should also be targeted for mass treatment (WHO, 2001).

1.4.2. Soil-transmitted helminths

The four most prevalent soil transmitted helminths (STH) species worldwide are: *Ascaris lumbricoides* (roundworm) *Trichuris trichiura* (whipworm) *Ancylostoma duodenale* and *Necator americanus* (hookworms). In case of *A. lumbricoides and T. trichura* eggs are deposited in the faeces and then into the environment. These eggs can be ingested through contaminated food or through dirty hands. For hookworm the larvae penetrates the skin of human directly from the infested soil. STH infections morbidity status varies and is dependent on intensity [50]. Some of the effects of STH include impaired growth and development of children. Studies indicate that the diseases affect one third of the global population with over 300 million people having chronic manifestations [51, 52].

Diagnosis of Hookworm and Trichuris infections is commonly through the same method used for *S. mansoni* infection. This is through counting the number of eggs per gram of faeces using direct smear and the Kato Katz technique. The major aim of control activities is to reduce morbidity control through treatment of at-risk populations to reduce the intensity of infection and protect infected individuals from further morbidity (WHO, 2010). Encouraging healthy behavior such as, hand washing and using latrines as well as provision of safe water are other important control measures for STH control [68]. Treatment is either with a single tablet of albendazole (ALB, 400mg) or mebendazole (MEB, 500mg). ALB can be safely co-administered with ivermectin (IVM) for the treatment of lymphatic filariasis and ALB or MEB can be safely co-administered with PZQ for the treatment of schistosomiasis. Mass treatment is delivered once or twice a year depending on the underlying endemicity with therapeutic coverage of 75% and above in SAC (WHO 2006).

1.4.3. Lymphatic filariasis

Lymphatic filariasis (LF) is caused by long thin filarial worms (*Wuchereria bancrofti, Brugia malayi and B. timori*) that live in lymph vessels in the human body and are transmitted by mosquitoes of *Anopheles, Culex, Aedes* and *Mansonia* genera [53]. Worldwide, the infection with *W. bancrofti* is the most wide spread of the human lymphatic filarial parasites and it is the only one transmitted in Africa [53, 54]. Transmission between humans and mosquitoes takes place when mosquitoes take a blood meal. Microfilariae (mf) are produced by the female adult worms in the lymphatics. They migrate to the blood system where they circulate and may be ingested by mosquito vectors. In the vectors they develop through various larval stages to an infective stage-L3. The infective stage larvae infect humans and migrate to the lymphatics where they develop into adult male and female worms. Adult worms have a life span of up to 20 years (but have been estimated to have an average life span of 5-12 years) while the mf may survive for approximately one year.

Several clinical features characterize LF. Some individuals may exhibit no obvious clinical manifestations though they are infected. Clinical manifestations begin with acute attacks characterized by fever, general body malaise and enlarged painful lymph nodes. This acute attacks are known to occur at irregular intervals [53, 55]. Chronic manifestations of LF include hydrocele (which affects men) and lymphedema or elephantiasis (which affects mainly the limbs of both males

and females). Women have also been known to have filarial infections of the breast and genitalia, although these are very rare. Chyluria, which presents a secretion of a milky like urine, is also acknowledged as one of clinical complications due to LF. About 5.5% of people affected by LF are known to have this complication in Niger Delta [56].

Lymphatic Filariasis is a disease of major public health importance which affects an estimated 120 million people worldwide; of which 44% are in sub-Saharan Africa [7, 57]. Although LF is not associated with any significant mortality, its debilitating chronic complications (hydrocele, lymphedema and elephantiasis) causes significant suffering and social stigma to the affected individuals and impedes economic performance of endemic communities [58]. Lymphatic filariasis is found mainly in remote rural areas and in some urban or peri-urban areas, where due to unplanned expansion of towns and cities, significant proportions of population have been forced to live in slums where mosquito breeding sites are a common feature [59]. This coupled with the heavy toll exerted by the chronic nature of the disease perpetuates the predicament at the individual level and endemic communities at large [60]. Acute attacks and microfilaremia is higher in early age groups with an increased risk in males; while elephantiasis and hydroceles manifestations are more common in older population [61-63].

Current methods for LF diagnosis rely on detection of circulating filarial antigens (CFA) in the blood, tested against the gold standard for diagnosis of detecting mf in the blood. The CFA are metabolic products released by adult worms. Detection of CFA indicates presence of adult worms. Given the fact that infected individuals have adult worms but no mf, the prevalence of CFA is usually much higher than the prevalence of microfilaraemia [64].

Efforts to effectively control LF have evolved through several decades. Developments in new diagnostic tools and treatment strategies have made the possibility of controlling LF appear more likely [54]. In 2000, the Global Programme to Eliminate Lymphatic Filariasis (GPELF) was launched following recommendation by the Task force for Disease Eradication World Health Assembly and the Resolution of 1997 WHA 50.29. The aim of the Programme is to eliminate LF as a disease of public health and socio-economic concern by the year 2020. The first component of GPELF is to interrupt transmission with annual single dose of albendazole in combination with either DEC or

ivermectin. This should be offered to all eligible populations in endemic communities in order to suppress microfilaraemia by killing circulating microfilariae produced by the adult worms and thereby preventing transmission. The drug combinations have other ancillary benefits in providing treatment of intestinal helminth infections [65]. For effective elimination of LF it is crucial that a high proportion of eligible persons in the community receive the single annual doses for a period of at least 5 to 6 years. Repeated rounds of treatment with high drug coverage are therefore required to reduce the infection and disease burden related to LF. The recommended period of 5 to 6 years corresponds to the reproductive lifespan of the adult parasitic worms [54]. The second pillar of the program refers to care for those already affected by manifestation of the disease. This is a crucial component in relieving individual suffering; which to some extent; increase drug uptake during MDAs [66].

1.4.4. Onchocerciasis

Human onchocerciasis (river blindness) is a helminths disease of humans caused by *Onchocerca volvulus.* It is characterized by skin and eye lesions. The parasite is transmitted through the bite of infected female black flies (*Simulium damnosum* s. l. and *S. neavei* s. s.) which breed in fast flowing rivers and streams. The disease manifests mainly as onchocercal skin disease characterized by severe itching and skin lesions. Itching can be so severe that it disturbs sleep, concentration and work [67]. The disease is endemic in 37 countries in sub-Saharan Africa, South America and 2 Arabian countries [68].

Approximately 42 million individuals are estimated to be infected with *O. volvulus* of which there are 13.1 million cases of severe itching and 385,000 cases of blindness as a result of the disease [69].

Early attempts to address the disease in Africa focused on vector control by spraying river banks. The Onchocerciasis Control Programme in West Africa (OCP) which was based on vector control was successful in eliminating the diseases from ten endemic countries in West Africa. The intervention was used in some foci in Tanzania, Uganda and Equatorial Guinea and was reported to be effective. Implementation costs were found to be the major barrier. Following on from the success of OCP the African Programme for Onchocerciasis Control (APOC) was established in year 1995 with the main objective of eliminating onchocerciasis as a public health problem in non-OCP countries. The

Programme was based on annual community-directed treatment with ivermectin (CDTI) as the main intervention in most areas except in a few foci where semi-annual treatment is implemented. In the America, semi-annual ivermectin treatment with a minimum coverage of 85% is the main intervention; but recently, quarterly treatment has been implemented in some foci. Recent findings have shown the possibility of elimination of onchocerciasis in most countries and a Guideline for Stopping mass drug administration and verifying elimination of human onchocerciasis has been adopted [69].

1.5. Neglected Helminth Infections in Tanzania

Tanzania is endemic for a number of neglected tropical diseases including onchocerciasis, lymphatic filariasis (LF) schistosomiasis, trachoma, soil transmitted helminthiases, Human African Trypanosomiasis, rabies, plague, echinococcosis, cysticercosis and brucellosis. Four of the diseases (onchocerciasis, lymphatic filariasis, schistosomiasis and intestinal helminthiases) are helminths and are under preventive chemotherapy control for which the mass drug administration has been adopted. Previously, these diseases were controlled through individual vertical programmes (MoH, 2010). The helminth infections that were focused on included LF, STH and schistosomiasis with limited (phased approach) MDAs implementation. For onchocerciasis treatment had been on-going in focal areas for several years before the surveys. MDA for the studied diseases i.e LF, STH and schistosomiasis were initiated in the selected districts.

In Tanzania Schistosomiasis is endemic country wide with very high prevalence of over 50% in over half the country, particularly in the six regions around Lake Victoria and in the four coastal regions including Dar es Salaam, Zanzibar and Pemba. Control has been targeting School Aged Children (SAC) with annual or biennial treatment with Praziquantel (40mg/kg) for high-moderate and low prevalence districts respectively.

STH are endemic in 80% of the country with a predicted prevalence of between 20-49% in most of the country reaching over 50% in some parts. School age children are targeted for control efforts due to the high prevalence of STHs among that group. The main intestinal parasites include hookworm, whipworm (*Trichuris trichiura)* and *Ascaris lumbricoides*.

Lymphatic filariasis is endemic in the whole of mainland Tanzania. Rapid mapping for lymphatic filariasis (LF) completed in Tanzania in 2004 indicated that all districts in the country are endemic. The circulating filarial antigen (CFA) prevalence ranged between 1%-69% with high prevalence along the coastal areas and decreases towards the inland [70]. Mass control of LF began formerly in year 2000 with the launching of the Tanzania Lymphatic Filariasis Elimination Programme (NLFEP). The elimination strategy is based on once yearly administration of two single dose drugs namely; ivermectin (150 µg/kg and albendazole (400mg); administered together. NTD programme report indicate that the number of districts requiring MDA has come down from 101 districts in year 2014 to 47 districts in year 2017 based on transmission assessment surveys (TASs) results. In case of patient care, activities are designed to establish community home-based self-care for people with lymphedema and to provide access to surgery for men with hydrocele.

1.5.1. Helminth Infections and co-endemicity in Tanzania

Helminth infections and their comorbidity have been studied in a number of settings with most studies focusing on STH and schistosomiasis [71, 72]. Studies in Tanzania indicated that individuals with multiple species infections are likely to be at the highest risk of geohelminths-related morbidity, not only because of the number of infections they harbor, but also because they generally carry heavier infections of each species [73-76]. Prevalence of single and multiple species helminth infection in school children revealed that *S. haematobium*, hookworm and *S. mansoni* were the most common helminths affecting school children. It was also found out that hookworm and *S. mansoni* occurred more frequently in multiple infections with other infection than as single species infection [76]. The relationship between HIV, lymphatic filariasis, malaria (Plasmodium falciparum) and intestinal helminths (*Ascaris lumbricoides*, *Trichuris trichiura* and hookworm) showed that hookworm infection was positively associated with *W. bancrofti* (CFA) infection and malaria but, surprisingly, a negative association with HIV infection. This situation was associated with a significant reduction in haemoglobin concentration [77].

1.5.2. Integration of helminth Control and elimination in Tanzania

The Neglected Tropical Diseases Control Programme was established in 2009 in-line with the WHO recommendation for NTD control in the African region. It works with local government authorities at regional and district level to provide Preventive Chemotherapy (PCT) services; among other things; to the affected communities. The neglected Tropical diseases targeted by PCT in Tanzania include; Lymphatic Filariasis, Schistosomiasis (SCH) and soil transmitted Helminthiasis, Onchocerciasis and Trachoma. Tanzania is one of the first WHO African regional countries to integrate the coordination and implementation of the 5 PCT-NTDs diseases control/elimination activities, including MDA, health education and morbidity management.

Results of mapping and several surveys of these helminth infections have shown that prevalence and intensities of infection differ from one place to another despite the overlap. Recently, Tanzania has moved towards integrated approach of the NTDs whereby, most/all NTDs activities are coordinated under one umbrella (the NTD program). This integrated approach is aimed at reducing duplication, maximizing the effect of control/elimination of the NTDs and ensuring prudent use of the available meagre resources. ,

Prior to 2009 all control and elimination efforts of the helminth diseases were conducted by separate programmes namely; Schistosomiasis and soil transmitted helminth control programme, National Onchocerciasis Control programme and the National LF elimination Programme. In year 2009 implementation of the integrated MDA approach was established. It started with the MDA in 36 districts endemic for more than 2 NTDs including the helminth infections. Upscaling to more districts was carried out in phased approach. In 2012 more districts were added to reach 92 and by year 2015 the country achieved full (100%) geographical coverage. For onchocerciasis full coverage was attained by 2009, for LF in 2014 and for STH and SCH in 2015/16.

2. RATIONALE AND OBJECTIVES

2.1. Rationale

Control of schistosomiasis, soil-transmitted helminthiasis (infections with *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm) and elimination of lymphatic filariasis is largely dependent on preventive chemotherapy (PCT). For all of these helminth diseases, donated or affordable drugs are available for effective prevention and control. These drugs, when used in preventive chemotherapy, have the power to interrupt transmission of burden caused by these ancient scourges of humanity. Control/elimination of these diseases coordinated and implemented through the Ministry of Health and education to reduce the disease burden to a level that they will no longer be of public health problem in the respective communities. Implementation of the programs is organized at district level and is included in the Comprehensive Councils health plans (CCHPs) which are prepared on annual basis.

Through the national programme, control of NTDs in an integrated approach was adopted in 2009 whereby, the MDA of these diseases using a combination of drugs that have so far been used was initiated. However, despite the already growing recognition of the role of multiple infections, and the fact that integrated control is taking place in some countries including Tanzania, it was unclear how the combined mass treatments would affect the population dynamics of the multiple species and overall helminths infection status in endemic communities. In essence, the fact that very few studies have sought to investigate multiple infection patterns and population dynamics; the dearth of information on how MDA alters the effects of polyparasitism; and the paucity of knowledge regarding the significance of polyparasite infection in parasite induced morbidity, contributed greatly to the lack of clarity pointed above.

Therefore, this study was carried out in 2 surveys one in 2013 and another one in 2014. Information collected included STH, schistosomiasis and LF infections with health indicators such as anaemia nutritional status and allergy surrogate marker prior to MDA and after round of MDA. It is envisaged that preventive chemotherapy for helminth have a significant impact on these indicators.

2.2. Research Question(s) and/ or Hypotheses

- Does preventive chemotherapy have impact on the overall helminth infections and its associated health indicators in selected urban and rural areas?
- Is there any effect on polyparasite infection and its associated health indicators after rounds of PCT/MDA?
- Is there a relationship between helminth infections and atopic diseases?

2.3. Study Objectives

The main purpose of this study was to determine the health impact of integrated preventive chemotherapy on selected NTDs in urban and rural endemic districts of Tanzania. Specifically, the study aimed:

- To determine the impact of preventive chemotherapy on helminth prevalence, intensities and associated health indicators in rural and urban areas.
- To determine the prevalence of polyparasitism helminth infections and its associated health indicators before and after MDA and morbidity in rural and urban areas.
- To determine the association of helminth infections and atopic disease in rural and urban areas.

3. METHODS

3.1. Study Design

Follow up surveys were conducted in 2013 and 2014 to determine the health impact of integrated preventive chemotherapy on LF, SCH and STH infections through prevalence and intensity. The districts were purposively selected based on the findings from the estimates of the Mapping surveys conducted by the Ministry of Health through its programmes as well as limited MDA.

In Kwimba, Sengerema, Temeke and Kinondoni districts, baseline data was collected in year 2013 and included participants 5 years and above. Moreover, in all the surveyed districts the baseline data was collected prior district-wide MDA.

Mass drug administration was conducted at least once in all surveyed districts soon after baseline data collection. It included administration of praziquantel and albendazole to all school aged children for SCH and STH control. Ivermectin and albendazole tablets were administered to all people above 5 years of age for LF in all surveyed districts except Kwimba and Sengerema, (*figure 3.1)*. Moreover in 2014 survey in Kwimba, Sengerema, Temeke and Kinondoni, the effect of helminth treatment on atopic diseases was assessed.

3.2. Study population and Area

Tanzania is situated in the East of Africa located between 6.3690^0 S and 34.888^o E has an areas size of 947,303 Square Kilometer .The country has a population of 51.8 million with 26 regions and over 160 districts [78]). In year 2013 baseline was collected from 4 districts in 2 the regions of Dar es Salaam and Mwanza namely Kwimba, Sengerema, Temeke and Kinondoni .These districts had not initiated district-wide MDA by 2013. Follow up was conducted in the same districts.

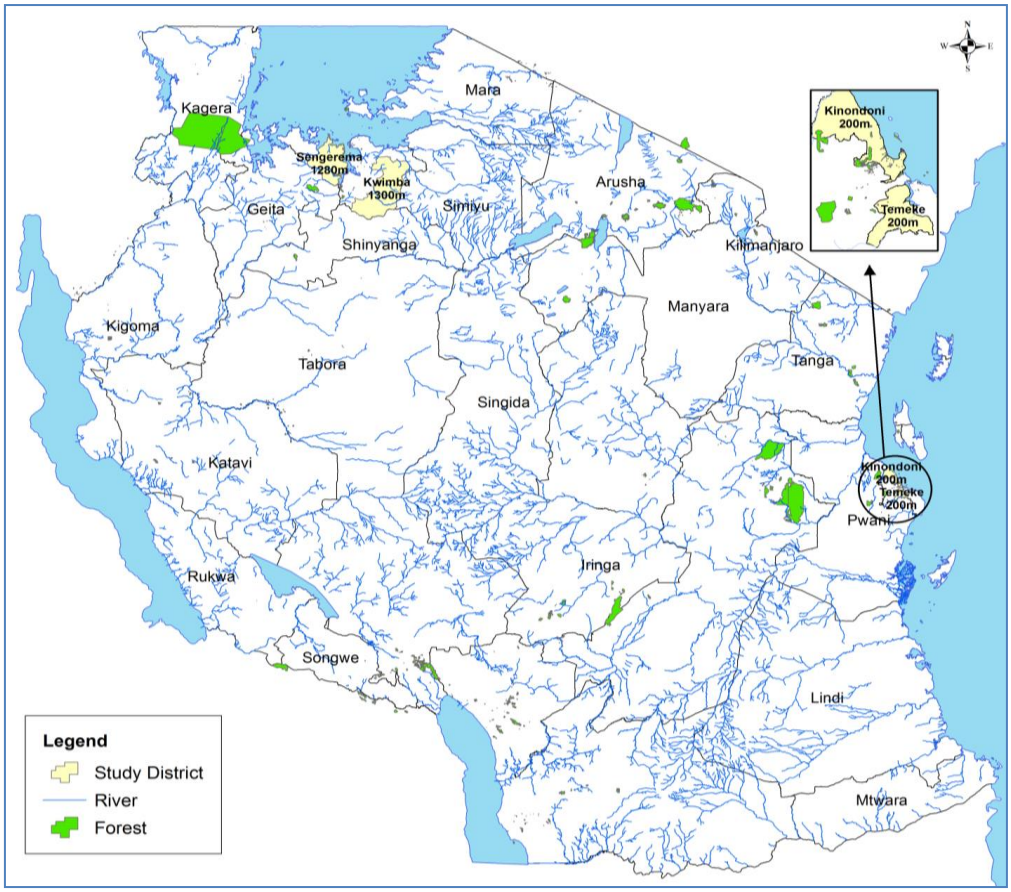

Figure 3.1: Map of study sites

3.3. Study Sites

3.3.1. Kwimba District

Kwimba district is one of the eight districts in Mwanza region near Lake Victoria. The district lies between latitude 2^{O} 45‟ to 3^{O} 53‟ south of the equator and longitude 33^{O} to 33^{O}·30‟ east of Greenwich. The district occupies an area of 3,903 km^{2} of land. The district has no water surface area, since it has neither lakes nor permanent rivers. Kwimba district lies between 1000m to 1200m above sea level. It has a moderate warm climate, with temperatures varying between 25^{O} and 33^{O} throughout the year. According to the Nation Population and Housing Census of 2012, the district had a population of 406,509 of which 198,096 were males and 208,413 were females with an annual average growth rate of 1.9%, population density of 104 people per square kilometer and a population size of 6.5. The district had a total of 62,540 households, of which 49,251 were in rural

areas and 13,289 were in urban areas. The district is composed of 5 divisions, 30 wards, 119 registered villages and 802 sub-villages [79].The study was conducted in Ngudu and Sumve wards. Health services in the district comprise a network of 2 hospitals, 5 health centres and 51 dispensaries under the ownership of government and private institutions. The district's social economic activities include agriculture, animal husbandry and petty businesses. The proportion of population with access to water supply is 58.7% only. The known endemic NTDs in the district are STH and SCH with the SCH average prevalence estimates from mapping surveys being 38.8. % and 1.4% for SCH and LF respectively [70, 80]. The Implementation of PCT started in year 2013 whereby, praziquantel and albendazole were administered to school aged children with coverage of 74 percent (74%).

3.3.2. Sengerema District

Sengerema district is also a district in Mwanza region. It lies between 2 ^{o} – 3^{o} latitudes South of equator and 31^{o} 45' to 32^{o} 45' longitudes. Sengerema district has a bimodal rainfall pattern which consists of a short and long rains. The annual rainfall ranges from 800mm – 1200mm. The District mean temperature is between 21^{o}C – 23^{o}C with August being the hottest months. The District covers an area of 8,817 sq. km of which 3,335 sq. km is mainland, while 5,482 sq. km (62% of the total area) is covered by Lake Victoria where numerous islands are found. Administratively, Sengerema District is divided into five (5) divisions, 34 wards, and 126 registered villages also comprises of 765 hamlets of which 52 make the Sengerema township authority [81].The study was conducted in Busisi and Bupampwa wards.

Health service Provision is comprises of District Designated Hospital (Faith Based Organization) 9 Health centers 56 Government dispensaries, 2 Private and 4 Faith based organization dispensaries. The major occupation is agriculture, livestock and fishing. East to the North Western part of the district there exist land slopes associated with a number of small hills and seasonal streams (rivers). Seasonal streams are also found in the eastern part of the district. Physical features of the district include also a number of manmade water bodies mainly dams of Sengerema, Buzilasoga, Sima, Nyamizeze, Nyakasungwa, Nyampande and Sotta. Sengerema District is characterized by an altitude which ranges between 900m – 1300m above sea level. By the year 2013, the District has been estimated to have total population of 711,632, of which 351,442 are males and 360,190 are females, with annual growth rate of 3.6%. This population is divided into five (5) divisions.

Sengerema had the LF prevalence of 5.3% and 23.8 % or Schistosomiasis at mapping around year 2005[70, 80]. STH is also endemic in accordance to hospital records. The Implementation of PCT started in 2013 whereby praziquantel and albendazole were administered to school aged children with coverage of 64 percent (64%).

3.3.3. Temeke Municipal Council

Temeke Municipal Council is one of the five Municipalities within the Dar es Salaam City; the others are, Kigamboni, Ubungo, Ilala and Kinondoni. It is the largest in size compared to Ilala and Kinondoni Municipalities. It covers an area of 656km² with a coastal line of 70km length. Temeke Municipal Council lies in the Tropical coastal belt of Tanzania. It is therefore, influenced by three major climatic seasons, namely the long and short rains and the dry season which is characterized by high temperature. .High temperature prevails throughout the year ranging from 25^0c during the period of June to August up to 35^0c in the period of January to March. According to 2012 Census the current population is estimated to be 1,611,972. Administratively, Temeke Municipal Council is divided into 3 divisions namely; Chan'gombe, Mbagala and Kigamboni. The divisions are further divided into 30 wards; which are also divided into 180 hamlets. The study was conducted in Yombo vituka and Mjimwema wards. Health service delivery at the Municipal Council is based on preventive, promotive and curative care provided to the community at Dispensary, Health Centre and Municipal Hospitals. They are supervised by the Municipal Medical Officer of Health. The Council has 123 Health facilities, 41 are owned by Government and 82 are privately owned. The public health facilities comprise 2 Hospitals (Temeke and Vijibweni), 1 Health Center (Kigamboni). NTDs endemic are LF, STH and SCH following previous prevalence surveys. Two rounds of MDA were conducted in 2006 and 2007 but were stopped due to unavoidable factors. MDA was restarted in 2013 whereby albendazole and ivermectin were administered to the population aged 5 years and above while Praziquantel followed only to school aged children. Coverage rates were 53% and 42% for LF and SCH respectively.

3.3.4. Kinondoni Municipal Council

Kinondoni Municipal is within the City of Dar es Salaam with an area of 531Km and population is about 1,775,049 (census 2012) with the increasing projection of 2,330,934 and population density is estimated at 2,051 person per square kilometer[82]. The Municipality is bordered by the Indian Ocean to the North East, Ilala Municipal to the South, Bagamoyo district to the North, Kibaha District to the west and Kisarawe district to the southwest. Administratively is dived into four (4) divisions namely: Magomeni, Kinondoni, Kibamba and Kawe. These divisions are then divided into 34 wards which in turn are sub divided into sub wards commonly known as 197 hamlets. The study was conducted in Bunju and Tandale wards. Kinondoni has well established healthcare system which provide both curative and prevent measure, it has a total number of 283 HFs both public and private in the following categories 19 hospitals, 13 health centers and 251 dispensaries. The social economic activities include working in (private and public sectors) petty trading, livestock keeping, fishing and agriculture. PCT diseases endemic include LF, SCH and STH and MDA was restarted in 2013 with coverage of 86% for ivermectin and albendazole while Praziquantel coverage was 49%.

3.4. Sampling

In the 2013 survey, study districts were purposively selected based on mapping survey estimates. Kinondoni and Temeke were chosen due to comparatively high prevalence rates for LF. Sengerema and Kwimba were also selected due to high SCH prevalence. Two urban wards were purposively selected from Temeke and Kinondoni districts. Two rural wards from Kwimba and Sengerema districts were also selected through purposive sampling. The districts and wards were selected based on findings from mapping surveys. In each ward two schools and its surrounding streets/villages were randomly selected Village/school were selected). In each school 50 children from grade 3 and 4 were enrolled .In the school surrounding areas, participants were selected from all hamlets and streets based on Population Proportionate Estimated sampling (PPES). A list of households was obtained from the hamlet office, and where this was not available, it was generated for survey purpose. The proportion of the population size of each street/hamlet for each ward was used to determine the required number of individuals to be surveyed per street/hamlet. An average household size of 5 people per household was used to determine the required number of households

to be surveyed in each hamlet. Sampling interval was determined by dividing total number of household in the ward by the number of households required from PPES. The starting point was selected using simple random number table. Then a sampling interval was applied to select subsequent households surveyed. In each household all members 5 years and above were enrolled for the survey.

In the Impact surveys, conducted in 2014, sampling followed the same approach used in 2013 (figure 3.2) in all study sites in the 4 districts of Kinondoni, Sengerema Kwimba and Temeke.

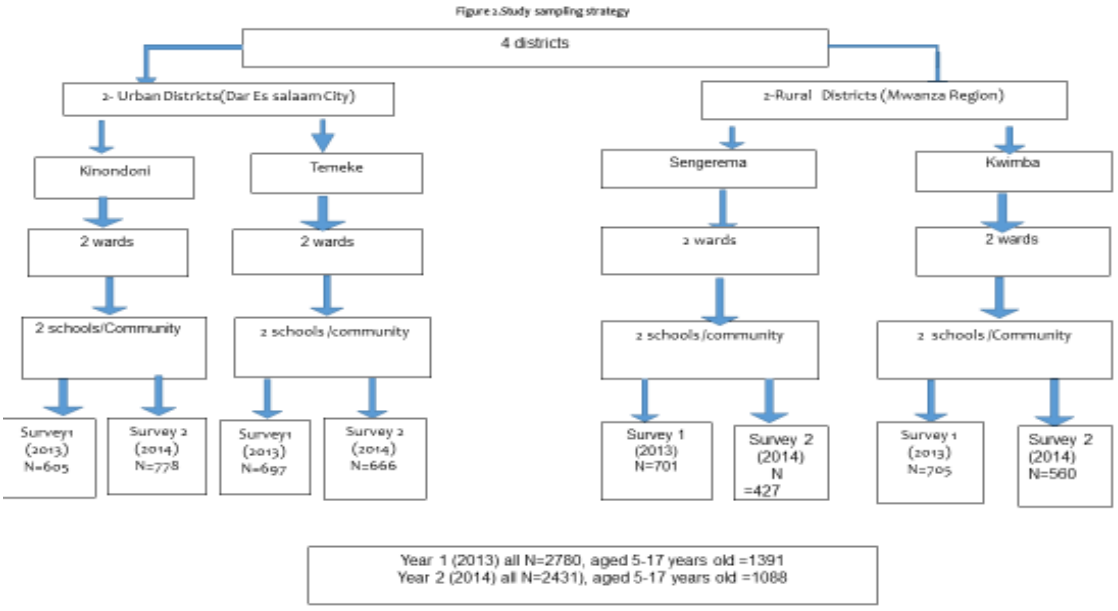

Figure 3.2: Study Design

3.5. Sample size calculations

The sample size calculation was based on the determination of whether the prevalence of multiple infection at in year 2013 prior to the implementation of MDA in study sites is different from the prevalence of multiple infection after one round of MDA in year 2014 assuming that the matching ratio of samples size between the two group is 1:1. The calculations assumed the prevalence of multiple infection in year 2013 to be 35% in the study in each study site (ward) and wanted to see a reduction in prevalence in multiple infection of helminths in the year 2014, to 25% after one round

of MDA. A 95% confidence level was needed to detect a significant difference between the two prevalence of multiple infection. A power of 80% was set for detecting the effect size.

Therefore the required sample size was calculated using following formula [83]

$$n = (Z_{1-\alpha/2}+Z_{1-\beta})^2 * (p_1(1-p_1) + p_2(1-p_2)) / (p_1-p_2)^2$$

Where: $Z_{1-\alpha/2}$, for 95% confidence level α is 0.05 and the critical value is 1.96. $Z_{1-\beta}$ for a power of 80%, β is 0.2 and the critical value is 0.84 and p_1 (0.35) and p_2 (0.25) are sample prevalence of the two groups. We estimated that a sample size of 326 per study site (ward).

3.6. Data collection methods and procedures

Data was collected on the following variables; Geospatial, biodata, anthropometric, and parasitology data as follows:

3.6.1. Geospatial data

Data was collected using GPS machines Garmin eTrex® where by a machine was set to record data at 5% precision .Variables on latitudes, Longitude and well as altitude was recorded. Point of references included types of water sources, forest, village center, school, health facilities and other prominent features. This was collected with aim of correlating the features with the helminth infections distribution.

3.6.2. Biodata:

This included sex, age, name of examinee, household head and place of residence (name of the village/street, district and region). Standard anthropometric included: weight, height and Mid Upper Arm Circumference (MUAC) and were measured using tape measure and weighing scale respectively. Height was measured in Centimeter (Cm) while weight was in kilograms (Kg) Mid Upper arm Circumference was measured in all SAC to determine their nutritional status. This was done to selected SAC in 2013 and 2014 data only.

3.6.3. Parasitological Examination:

Special trained technicians collected and processed blood, urine and stool samples and the following procedures were conducted:

3.6.3.1. Blood

100 microliter was drawn into heparinized capillary tube and was placed on ICT card (BINAX NOW®) for detection of Circulating Filarial Antigen (CFA), specifically a capillary was placed on pink pad of the Card. Thereafter, the card was closed and labelled with ID of the individual. Time of blood application to the card was also recorded on top of the card. Results were read after 10 minutes in accordance to manufacturer's instructions.

Thick thick/thin smear (blood slides) was done for Malaria and other significant blood parasite was checked microscopically for authenticity of anaemia and or fever cause.

Haematological investigation (Hb and eosinophil count respectively). Approximately 1 ml of blood was collected in the EDTA tubes and was analysed using haematology analyser MS59s.

3.6.3.2. Stool samples

Stool samples were collected within 24 hours of defecation and analysed in the field laboratory as well as at central laboratory. It was analysed visually for consistency where it's formed, non-formed, loose, mucoid or bloody.

Prevalence and intensity of geohelminths and *S. mansoni* ova was determined using Kato Katz technique [84]. The stool sample was processed immediately while still fresh. A small portion of stool from the sample container using a wooden spatula was taken from the container and smeared on a sieve and transferred to the slide templates. A piece of prepared cellophane with forceps was placed over stool each slide's specimen. The slides were quantitatively examined under microscope then within one hour for hookworm ova. After at least 24 hours, the slides were quantitatively examined under the microscope for S. mansoni, Ascaris lumbricoides and Trichuris trichiura ova.

3.6.3.3. Urine sample

The urine was collected in containers from the client and examined visually. Dipstick test was performed for testing blood in urine ; one half of the reagent strip was dipped into the urine sample for a few seconds and compare the color of the reagent strip to the colors on the label of the reagent strip container. Results were written on the laboratory form provided.

Filtration technique was used for the detection of *S haematobium* ova: Urine was collected in a sterile container and the urine sample thoroughly mixed, 10 ml of urine was drawn using a syringe. Thereafter it was passed the through the filter and remove the syringe from the filter holder. The filter was placed on a glass slide and quantitatively examined under the microscope for *S. haematobium* ova. The number of eggs was recorded on the laboratory form.

3.6.4. Skin Prick tests

For allergic tests, skin prick tests against HAL Dermatophytes (*D. farinae*, *D. pteronyssinus*) and cockroach allergens (*Blatella germanica*) were done. Histamine was a positive control and normal saline was a negative control. The tests were performed for each allergen with positive and negative control. The skin was coded with marks of the allergens and controls (negative and positive) then allergens were dropped on each point using a specialised dropper. Thereafter tiny pricks were made in the middle of each drop using HAL lancets. According to manufactures instructions, results were read after 15 minutes whereby any induration was recorded and measured[85]

Figure 3.3: Skin Prick Test

3.7. Data Management and Analysis

Data from the field was collected using structured questionnaire forms during the baseline survey. All data collected from the individuals enrolled into the study was entered and edited using Epi data software version 3.2. During year 2014 (impact) survey the structured questionnaire was administered through mobile phones using the Open Data Kit (ODK) software. This data was then transferred to STATA version 12 software for subsequent analysis. Data was analyzed to provide a picture on the distribution (prevalence and intensity) of STH, schistosomiasis and LF before and after the implementation of MDA in the selected districts.

3.7.1. Creating and defining variables for analysis

Prior to the actual analysis of data several variables were formatted in suitable ways according to the standard definition recommended.

Age reported by the participants was classified in 5 categories; 5-10 year, 11-17 years, 18-24 years, 25-49 years, 50 years and above. This classification is based on target to start PCT in those aged 5 years. This is because 5 to 17 is the school age in most of the study areas which is considered as the population at risk for at least 2 out of the 3 diseases of focus (schistosomiasis and STH) while age 18-24 year represent youth who are considered the most vulnerable for mosquito bites due to outdoor exposure to mosquitoes and social economic activities (relevant for LF and malaria); 25 years and above are adults and child bearing age included as risk group for all tropical infections.

Height and Weight-for-age z-scores (WAZ) among school children were calculated based on the WHO growth standards [86] .Participants with z-scores below -2 were defined as stunted and underweight. Binary variables of the infections were created, those individuals who were with eggs/CFA positives were termed as cases given the numerical number 1, and those who were found not having eggs/CFA negatives were termed as non-cases were given numerical number 0. Infection profile status was created by combining data on STH, SCH and LF for each individual to determine those with none, single, double, triple and multiple infections. "Any infection" was defined as presence of any infection among the three groups of the mentioned helminth infections. This was important due to the multiple effects of the anthelminthic medicines (albendazole, ivermectin and praziquantel) on

the studied helminths. Prevalence of infections for each disease and its profile by area, age and sex was determined. The number of eggs counted in stool was multiplied by a factor of 24 to obtain the number of eggs per gram (EPG) (as the Kato Katz template allows the microscopy of exact 41.7 mg of stool). Geometric Mean Intensity (GMI) of STH and schistosomiasis infection was obtained by logarithms transformation on the number of eggs counted per gram.

Intensity of STH and schistosomiasis was classified according to WHO guidelines [87]. The classification of intensity for soil-transmitted helminths were as follows: *A. lumbricoides* (light (1-4999 eggs/g), moderate (5000 - 49999 eggs/g) and heavy (≥ 50000 eggs/g) of stool); *T. trichiura* (light (1-999 eggs/g), moderate (1000-9999 eggs/g) and heavy (≥ 10000 eggs/g) and *Hookworm (* light (1-1999 eggs/g), moderate (2000-3999 eggs/g), and heavy (≥ 4000 eggs/g)). *S. mansoni* was classified into light infection if eggs counts ranged light (1-99 eggs/g, and moderate infection if eggs count ranged 100-399 eggs/g and heavy infections more than 400 eggs/g of the stool (EPG).

S. haematobium was categorized as light infection if eggs counts in urine ranged 1-49 eggs/10ml and heavy infection if eggs count is greater than 50 eggs/10ml.

Anaemic individuals were classified as follows: Children age 5-11 years who had haemoglobin level (Hb) less than 11.5g/dL; those 12-14 years who had Hb less than 12g/dL; Non-pregnant women aged 15 and above who had Hb less than 12g/dL and men aged 15 and above who had Hb less than 13g/dL[88]. Eosinophilia was defined as White Blood Cell (WBC) counts which is greater than 7% of eosinophilic leukocytes [21]. An association of level of eosinophil count with single and multiple infections was determined.

For Skin Prick tests; Only SAC were tested in 2014 and only valid tests with positive and negative control were included in the analysis. Binary variables of the skin prick test were created for each allergen including positive and negative control, those individuals who had an induration of with diameter more than 3mm were termed as cases given the numerical number 1, and those who had an induration less then 3mm diameter were termed as non-cases were given numerical number 0 [89].

3.7.2. Determining the association between infection status and other variables

Both univariate and bivariate analysis were done to explore the data and finding out relationship between two variables. The degree of association was obtained using chi-square test at 5% level of significant (p-value<0.05). Multivariate logistic analysis taking districts under survey as the random effects was done to find out the effect of helminths infections on the risk of stunting, underweight and anaemia adjusted by age group, sex, area (urban vs rural) nutritional status and infection prevalence. Akaike Information Criterion (AIC) a tool that compares different models given the same data was used to select the model that best balances drawbacks**.** The model with the lowest AIC score was selected as a best fitted model [90]. Thereafter, null -hypothesis testing was used on the best model to determine the relationship between specific variables and the outcome of interest. Multivariate logistic regression results were considered significant for p<0.05.

For Skin prick test, a random effects logistic regression analysis was done. The analysis took into account the *D.farinae, D.pteronnyssinus* and cockroach allergen as the outcome variables and treated districts as the random effect of the model. This was done on the infection prevalence, areas of residency (rural/urban), sex and age of the study participants. Similar approach was used for selection of the best model as above.

3.8. Ethical statement

The proposal for this research was submitted to the Medical Research Coordination Committee (MRCC) of the National Institute for Medical Research-Tanzania for ethical and scientific approval. The study was reviewed and given an approval No. NIMR/HQ/R.8a/Vol.IX/1568 dated 8th July 2013. An Ethical waiver was also provided by LMU in German as per University's guidelines. Proposal amendment to include other districts was granted and extended to be valid till July 2017. Permission to publish these data was granted by the Director General, MRCC-NIMR, as per requirement indicated in Ethics Clearance Certificate.

District and village authorities were informed on the survey objectives, procedures, benefits and risks. A locally translated parental/guardian consent form was used. The form informed parents/guardians and participants about the nature of the study, and that their participation was voluntary. The multidisciplinary, gender balanced team was identified and trained on study methods

to avoid bias and influence. All interviews were conducted at a place and time that was convenient to both study participants and interviewers using Swahili language. Efforts were made to ensure privacy and confidentiality during the interviews.

3.9. Study limitation

Skin prick tests data planned to be conducted in 2013 surveys was not collected due to late importation of test kits from the manufacturer.

4. RESULTS

Results presented in this section include characteristics of study population, prevalence and intensity infections in urban and rural areas for survey 1 (2013) and survey 2 (2014). Moreover the association between helminth infection with nutritional status, anaemia and allergy are presented. For comparison reasons data included only individuals aged 5 years and above since that group was reached in all surveys and is the target group for preventive chemotherapy or MDA for the targeted diseases.

4.1. Characteristics of the study population by year of survey.

The demographic characteristics of the study participants in the four districts are presented in table 1a. In 2013, 2,708 participants were sampled while in 2014, 2,431 participated. Study participants' distribution by areas (rural and urban). In year 2013; 1406 (51.9%) were sampled from rural areas and 1302(48.0%) from urban areas. In year 2014, 987 (40.6%) participants were from rural and 1444 (59.4%) from urban districts. By gender 1,380 (50.6%) were males and females 1338 (49.4%). In year 2014; about 1052 (43.3%) were males and 1379 (56.7%) females, see Table 4.1.

Participants aged 5 years to 17 years old (including ages 5 and 17) were 1,391 (56.2%) and 1,084 (43.8%) in 2013 and 2014 respectively.

Table 4.1 Study population characteristic in year 2013 and 2014

Characteristics	Year 2013 n (%)	Year 2014 n (%)
Number of Participants	**2708**	**2431**
Rural	1406 (51.9)	987 (40.6)
Kwimba (rural district of Mwanza)	705 (26.0)	560 (23.0)
Sengerema (rural district of Mwanza)	701 (25.9)	427 (17.6)
Urban	1302 (48.0)	1444 (59.4)
Temeke (urban district of Dar es Salaam)	697 (25.7)	666 (27.4)
Kinondoni (urban district of Dar es Salaam)	605 (22.3)	778 (32.0)
Sex		
Male	1370 (50.6)	1052 (43.3)
Female	1338 (49.4)	1379 (56.7)
Age(n)		
5-10 years	611 (22.3)	778 (32.0)
11-17 years	780 (28.8)	306 (12.6)
18-24years	316 (11.7)	315 (13.8)
25-49 years	706 (26.1)	733 (30.2)
50 and above	292 (10.8)	297 (12.2)
Total	**2705**	**2429**
Study population 5-17 years, n (%)	1391 (56.2)	1084 (43.8)

4.2. Proportion of anaemia, eosinophilia and nutritional indicators by years of surveys

In year 2013, out of 1, 391 participants aged 5 to 17 years old, 1,054 (75.8%) were tested for haemoglobin level while in year 2014, out of 1084 participants 581(53.6%) were sampled for haemoglobin level test. In 2013, those sampled from urban areas were 647 (61.4%) while rural 407 (38.6%). In 2014; 340 (58.5%) were from urban and 241 (41.5%) were from rural areas. There was a notable change in mean haemoglobin from 2013 to 2014, whereby mean haemoglobin dropped significantly from 12.5 to 11.9g/dl, $p<0.001$ (table 4.2). The proportion of anaemic participants increased from 239/1,054 (22.7%) in year 2013 to 193/581 (33.2%) in year 2014.

Regarding anaemia a difference between the urban and rural areas was noted. In urban areas, the proportion of anemic participants dropped from 143/647 (22.1%) in year 2013 to 37/340 (10.9%) in year 2014, $p<0.001$ while in the rural areas, proportion of anemic participants increased from 96/407 (23.6%) in year 2013 to 156/241 (64.7%), $p<0.001$ in year 2014.

Two nutritional indicators were measured: Weight for age and height for age. No change for weight was seen from 2013 to 2014. Underweight children were found in 174/1,060 (16.4%) of the children in 2013 and in 156/829 (18.8%) of the children in 2014, $p=0.2$.

In contrast, a significant decrease proportion of stunted participants from 273/1,009 (27.1%) in year 2013 to 124/ 828 (15.0%) in year 2014, $p<0.001$, (Table 4.2).

Table 4.2 Proportion of participants tested for blood and anthropometric indicators by year of surveys in rural and urban areas

	Characteristics	Year 2013	Year 2014	Test Statistics &P value
Study population 5-17 years		1391	1084	
Number tested for Hb, n (%)		1054 (75.8)	581 (53.6)	
Areas	Urban n (%)	647 (61.4)	340 (58.5)	
	Rural (%)	407 (38.6)	241 (41.5)	
Mean Haemoglobin level: n (mean)		1054 (12.5)	581 (11.9)	t-test=7.6, p<0.001
Anaemia status n (%)	Normal	815 (77.3)	388 (66.8)	
	Anaemic	239 (22.7)	193 (33.2)	X^2_1 =21.4, p<0.001
Anaemia category=n (%)	None	815 (77.3)	388 (66.8)	
	Mild	143 (13.6)	107 (18.4)	
	Moderate	87 (8.3)	81 (13.9)	
	Severe	9 (0.9)	5 (0.9)	
only urban areas	**only urban areas**			
Mean Haemoglobin level: n (mean)		647 (12.69)	340 (12.63)	t-test=0.8, p=0.4
Anaemia status n (%)	Normal	504 (77.9)	303 (89.1)	
	Anaemic	143 (22.1%)	37 (10.9)	X^2_1 =18.8, p<0.001
Anaemia category=n (%)	None	504 (77.9)	303 (89.1)	
	Mild	91 (14.1)	19 5.6)	
	Moderate	46 (7.1)	81 (4.7)	
	Severe	6 (0.9)	2 (0.6)	
only rural areas	**only rural areas**			
Mean Haemoglobin level: n (mean)		407 (12.3)	241 (11.1)	t-test=12.4, p<0.001
Anaemia status n (%) rural	Normal	311 (76.4)	85 (35.3)	
	Anaemic	96 (23.6%)	156 (64.7)	X^2_1 =107.8, p<0.001
Anaemia category=n (%)	None	311 (76.4)	85 (35.3)	
	Mild	52 (12.8)	88 (36.6)	
	Moderate	41 (10.1)	65 (27.0)	
	Severe	3 (0.7)	3 (1.2)	
Eosinophilia (>7%)	Normal	714 (69.2)	411 (94.5)	
	High	318 (30.8)	24 (5.5)	X^2_1 =109.5, p<0.001
Nutritional status				
Weigh for Age (WAZ)	Normal	886 (83.6)	673 (81.2)	X^2_1 =109.5, p=0. 2
	Underweight	174 (16.4)	156 (18.8)	
Height for Age (HAZ)	Normal	736 (72.9)	704 (85.0)	X^2_1 =109.5,p<0.001
Stunted	Stunted	273 (27.1)	124 (15.0)	

Regarding eosinophilia, a potential surrogate marker for helminth infection, a significant drop from 318/1032 (30.8%) in 2013 to 24/435 (5.5%) in 2014 was noticed (p<0.001).

4.3. Prevalence of helminth infections by year of survey

A total 752 and 804 participants aged 5-17 years old were tested for stool in year 2013 and 2014 respectively while for urine the numbers examined were 749 and 804 in year 2013 and 2014 respectively.

4.3.1. Schistosoma haematobium infection prevalence

Overall prevalence in 2013 was 73/749 (9.8%). No cases were found in urban areas. In rural areas, 73/403 (18.1%) were infected. Further analysis of sex and age distribution was performed only for rural areas. The prevalence was higher among males' participants 47/369 (12.8%) compared to females 26/380 (6.8%) p<0.001. Age wise participants aged 11 – 17 years old had with 49/416 (11.8%) a higher prevalence compared to 5-10 years olds were 24/333 (7.2%), p=0.04 were S. haematobium were positive

In year 2014, 22 of the participants were found to have *S. haematobium* infection as before (all in rural areas) leading to a prevalence of 22/406 (5.4%). A significant crude reduction of 74% (95% CI 57%-84%, p<0.001) of *S. haematobium* infection from 2013 to 2014, was noted. The drop in prevalence was seen in all subgroups: Prevalence in males dropped from 47/369 (12.8%) to 9/ 386 (2.3%), reduction of 84% (95% CI 66% to 93.0%, p<0.001. Females dropped from 26/380 (6.8%) to 13/ 418 (3.1%), reduction of 57%, 95% CI, 14 to 78%, p=0.015. Among participants aged 11 – 17 years old the prevalence dropped from 49/416 (11.7%) to 9/199 (4.5%), p<0.001.The drop in prevalence of infection was also noted among participants 5-10 years old from 24/333 (7.2%) in 2013 to 13/605 (2.1%) p<0.001 in the year 2014.

4.3.2. Schistosomiasis mansoni infection prevalence

In 2013, overall 11/752 (1.5%) participants were infected. There was no case in urban areas. Participants from rural areas had a prevalence of 11/406 (2.7%), of these 11 infected 5/383 were females (1.3%) and 6/ 369 (1.6%) were males (table 4.3a). The difference in prevalence of infection between males and females was not statistically significant with p=0.5. Likewise there was no significant difference in infection among age groups (Table 4.3a).

In year 2014, overall there was no significant change in infection prevalence of *S. mansoni* from year 2013 (Table 4.3b).

4.3.3. Hookworm infection prevalence

In 2013, the overall prevalence of hookworm infection 21 /752 (2.8%).One 1 /346 (0.3%) was from urban and 20/ 406 (4.9%) were from rural areas, p<0.001. The infected participants in urban areas was a female in the age group 11-17 years old while those in the rural areas were evenly distributed: 10/182 (5.5%) were males, and 10/224 (4.5%) were females, p=0.6. Those aged 5-10 years were 8/ 193 (4.2%) and aged 11-17 years were 12/ 213 (5.6%), p=0.5. Therefore, neither gender nor age groups showed evidence on differences in prevalence of hookworm infection (Table 4.3a)

In 2014, overall 17/804 (2.1%) had hookworm infection indicating no significant drop from year 2013, where the prevalence was 21/752 (2.8%), p=0.4. In 2014, there were no participants infected in urban areas. Among the participants infected with hookworm of the rural areas, 8/207 (3.9%) were females and 9/199 (4.5%) were males (Table 4.3b).

Table 4.3a Prevalence of helminth infections in year 2013 by areas (rural /urban), sex and Age

		Areas		**Sex**		**Age**	
	Variables	**Urban**	**Rural**	**Female**	**Male**	**5 to 10 years**	**10 to 17 years**
	Total	346	403	380	369	333	416
S.haematobium	Cases	0	95	26	47	24	49
	Prevalence	0.0	23.6	6.8	12.7	7.2	11.8
	Test statistics	p<0.001		p=0.007		p=0.04	
	Total	346	406	383	369	335	417
S.mansoni	Cases	0	11	5	6	3	8
	Prevalence	0.0	2.7	1.3	1.6	0.9	1.9
	Test statistics	p<0.001		p=0.7		p=0.2	
	Total	346	406	383	369	335	417
Hookworm	Cases	1	20	11	10	8	13
	Prevalence	0.3	4.9	2.9	2.7	2.4	3.1
	Test statistics	p<0.001		p=0.9		p=0.5	

Table 4.3b: Prevalence of helminth infections in year 2013 and 2014 by district

Infection	areas		Year 2013	Year 2014	**Test Statistics &P value**
S.haematobium	Urban	Number examined	346	398	
		Cases	0(0.0)	0(0.0)	
	Rural	Number examined	403	406	X^2_1 =31.5, p<0.001
		Cases	73(18.1)	22(5.4)	
S.mansoni	Urban	Number examined	346	398	
		Cases	0(0.0)	0(0.0)	
	Rural	Number examined	406	406	X^2_1 =3.3, p=o.07
		Cases	11(2.7)	4(1.0)	
hookworm	Urban	Number examined	346	398	X^2_1 =1.2, p=0.3
		Cases	1(0.3)	0(0.0)	
	Rural	Number examined	406	406	X^2_1 =0.3, p=0.6
		Cases	20(4.9)	17(4.2)	
LF (all)	Urban	Number examined	1275	1358	X^2_1 =0.06, p=0.8
		Cases	29(2.3)	29(2.1)	
	Rural	Number examined	1406	963	X^2_1 =0.5, p=0.4
		Cases	16(1.1)	8(0.8)	

4.3.4. Malaria

The malaria tests were performed for the age group 5-17 years old.

In 2013, total 1,054 were tested for the presence of malaria parasites in their blood, out of these 10 (1.0%) were found to have malaria parasites from both rural and urban settings. Out of 647 tested were from urban and only 1 (0.2%) was found to be positive. The prevalence was 9/407 (2.2%) for the rural areas. There was no difference of malaria infection neither between age groups nor between males and females for year 2013.

In year 2014, a total of 648 participants were sampled and 62 (9.6%) of them were found to have malaria parasites. There was a 10 folds increase in the prevalence of Malaria in year 2014 compared to 2013, p<0.001. Moreover in 2014, all 62 positive cases were from rural areas, were the prevalence rose from 9/407 (2.2%) to 62/308 (20.1%) from 2013 to 2014. No sex and age group differences in prevalence of malaria were observed as in year 2013.

4.3.5. Lymphatic Filariasis (LF) infection prevalence

LF was tested in blood samples of individuals aged 5 to 92 years of age.

In 2013, a total 2,681 were tested for LF using CFA, out of these 45/ 2,681 (1.7%) were found to have positive antigenemia in both rural and urban settings, of these urban participants were 29/1,275 (2.3%) while rural were 16/ 1,406 (1.1%),p=0.02; indicating a higher prevalence of LF infection in urban areas than in rural areas. The prevalence of infection was not significant between males 27/ 1,360 (2.0%) and female 18/ 1,321 (1.4%) p=0.2. The prevalence of infection was noted to increase with age**.**

In year 2014, a total of 2,321 participants were sampled and 37/ 2,321 (1.6%) of them were found to have LF infection. No significant change of LF infection was observed between the 2 surveys in terms of areas of residence, and gender. Moreover in 2014, a total 29/ 1,358 (2.1%) were from urban areas while 8/ 963 (0.8%) were from rural areas, p=0.013. It was also noted that participants aged 18-24 years had a highest prevalence 14/305 (4.6%) compared to other age groups. (Figure 4.1 prevalence trend by years). Comparing the overall LF prevalence in year 2013, 45/2,681 (1.7%) and year 2014, 37/2,321 (1.6%) no major change was seen. However, separating between age groups an increase in LF prevalence from 6/313 (1.9%) to 17/305 (4.6%), p=0.06 was seen, and a decrease among the over 50 year olds from 11/290 (3.8%) to 3/294 (1%), p=0.003.

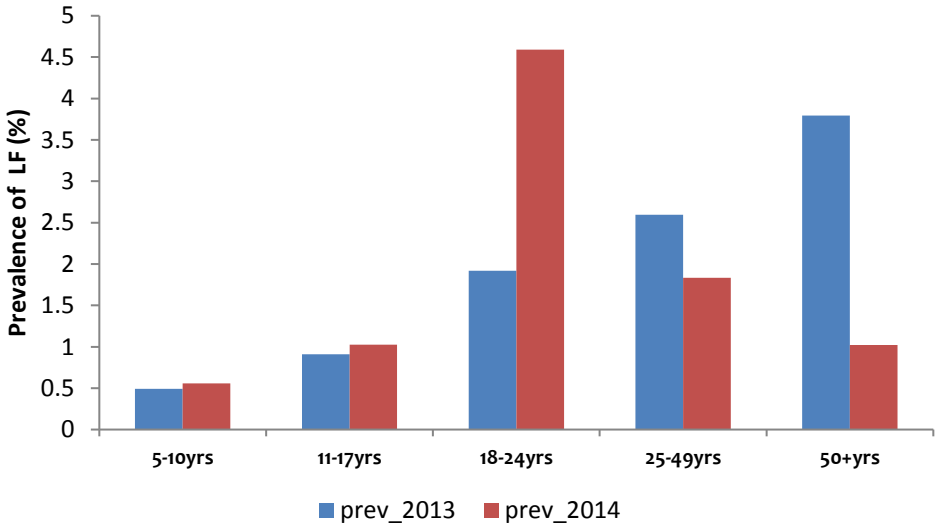

Figure 4.1: Prevalence of LF by age and year of survey

4.4. Helminth Infection intensity by years of surveys

4.4.1. *S. haematobium* intensity

Overall prevalence in 2013 was 73/749 (9.8%), 64/749 (8.5%) were categorized of having a light infection (between 1 and48 eggs/10ml of urine) and 9/749 (1.2%) were heavy infected (egg count between53 and 118eggs /10ml of urine).

Overall Geometric Mean intensity (GMI) in 2013 was 10.4 (95% CI; 7.7-14.1) eggs /10ml of urine among infected participants.

In 2014, GMI intensity was 7.8 (95%CI 5.4-11.2) eggs /10ml of urine among infected participants in rural areas. Findings revealed no overlap in confidence intervals indicating non-significant drop in intensity from 2013 to year 2014, p=0.1 (*Figure 4.2*). Moreover no heavy infected participants were found and those with light infections were 22/804 (2.7%).

4.4.2. S. mansoni intensity

S. mansoni infection was diagnosed in 11 participants in 2013, of which *four* 4/752 (0.5%) participants had light infection and 7/752 (0.9%) had heavy infection. The egg count ranged from 12/gram to 9600/gram with an overall GMI of 410.8 (95% CI: 85.4-1975.3) epg among infected participants.

In the year, 2014, all infected participants had light infections. The GMI was 40.4 (95% CI: 14-116.0) epg. The drop in GMI from year 2013 to 2014, was statistically significant, p=0.01 (*Figure 4.3).*

4.4.3. Hookworm Intensity

In 2013, Geometric Mean intensity of those infected with hookworm infection was 318 (181.3-558.3) epg. All infected had light infections.

In 2014, rural areas the GMI dropped to 70.7 epg (51.0-98.0) while no was infections were seen in the urban areas. Findings indicate a significant reduction in intensity of infections from 2013 to 2014, p<0.001 (*Figure 4.3).*

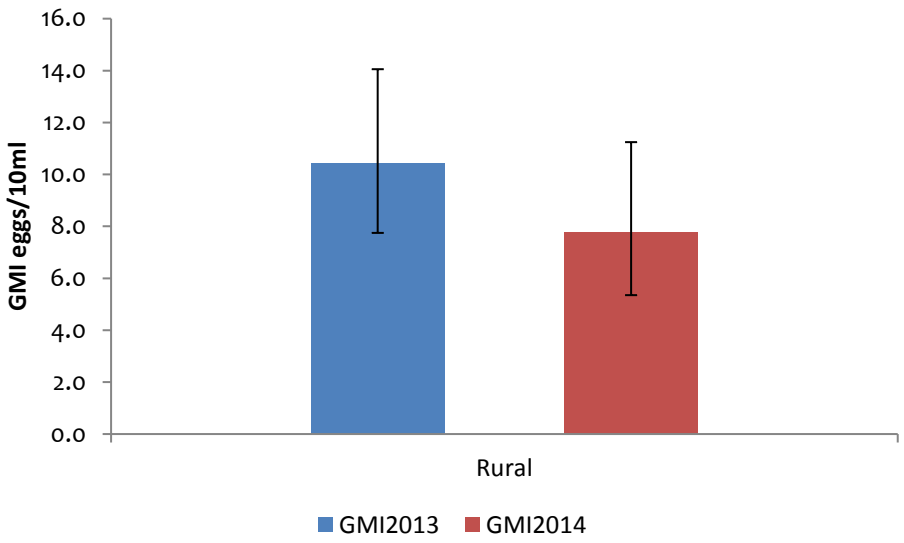

Figure 4.2: Intensity of S. haematobium in rural areas and by year of survey

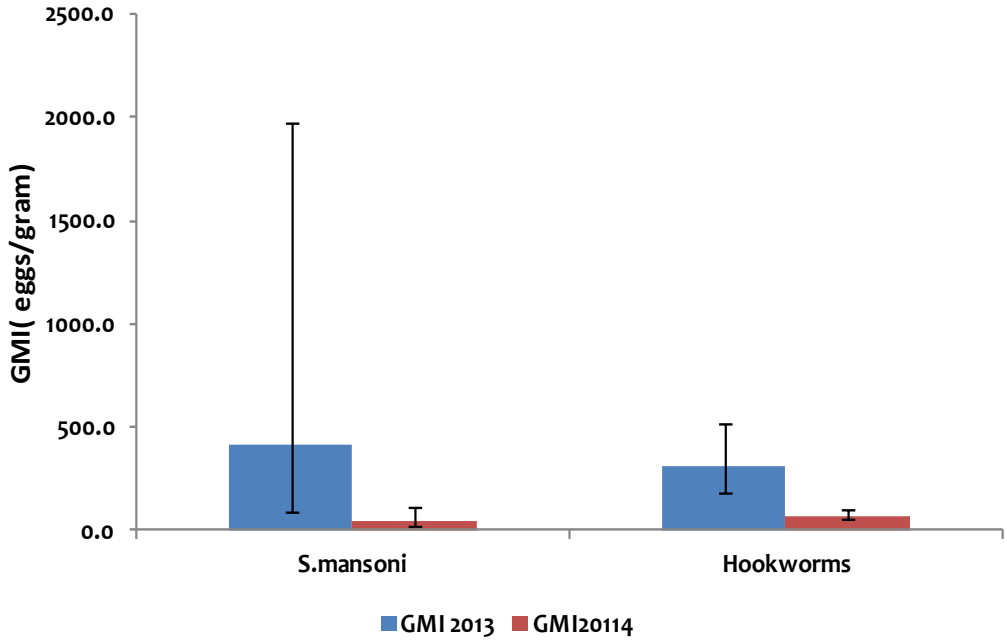

Figure 4.3: Intensity of hookworm and S. mansoni in rural areas by years of survey.

4.5. Nutritional Indicators and Anaemia before and after MDA (CRUDE).

4.5.1. Stunting before and after MDA

Compared to the findings observed in the 2013 survey the results regarding health indictors in the 2014 survey showed an overall prevalence of stunting among 770 participants tested to be 115 (15.0%) compared with the 165/746 (22.1%) stunted individuals in 2013, this represents a crude reduction of 38% (95%CI: 19-53%, p<0.001). The crude reduction of stunting in females and males was 37% (95%CI: 0. 6-57%, p=0.02) and 39% (95%CI 13-57%, p=0.006) in 2013 and 2014 years respectively, and with that no difference between the gender. There was no significant change in stunting between age groups between 2013 and 2014 surveys. The reduction was also noted in participants from urban and rural areas as shown in table 5a. However, there was no significant change observed in stunting among participants infected with *S. haematobium*, *S .mansoni* and hookworms (table 4.4a).

Table 4.4a: Stunting with helminth infection sex and age: Comparison of 2013 and 2014

Variables	Number examined	% positives (year 2013)	Number examined	% positives (year 2014)	Odds ratio	95% CI*	P value
overall	746	165 (22.1)	770	115 (15.0)	0.62	0.47 to 0.81	p<0.001
Sex							
female	380	70 (18.4)	400	50 (12.5)	0.63	0.43 to 0.94	p=0.02
male	366	95 (26.0)	370	65 (17.6)	0.61	0.43 to 0.87	p=0.006
Age							
5 to 10 years	333	43 (12.9)	582	59 (10.1)	0.76	0.50 to 1.16	p=0.199
10 to 17 years	413	122 (29.5)	188	56 (29.8)	0.95	0.69 to 1.48	p=0.95
Areas							
urban	344	70 (20.4)	394	49 (12.4)	0.55	0.37 to 0.83	p=0.004
Rural	402	95 (23.7)	376	66 (17.6)	0.69	0.48 to 0.98	p=0.04
S. haematobium							
negative	674	148 (22.0)	750	111 (14.8)	0.62	0.47 to 0.81	p<0.001
Positive	72	17 (23.6)	20	4 (20.0)	0.81	0.24 to 2.77	p=0.74
S. mansoni							
negative	735	161 (21.0)	768	114 (14.8)	0.62	0.48 to 0.81	p<0.001
Positive	11	4 (36.4)	2	1 (50.0)	1.75	0.07 to 41.7	p=0.73
Hookworm							
negative	725	156 (21.5)	754	110 (14.6)	0.62	0.48 to 0.82	, p<0.001
positive	21	9 (42.9)	16	5 (31.3)	0.61	0.15 to 2.44	p=0.48

4.5.2. Comparison of underweight before and after MDA.

In the 2014 survey the overall prevalence of underweight was 143 (18.6%) out of 771 participants indicating a crude increase in risk of underweight by 1.47 (95% CI 1.11.-1.96, p=0.006) times compared to year 2013. Among females the risk increased by 1.51 (1.0-2.28, p=0.047) times while among males the prevalence increased by 1.45%. (95% CI: 0.99-2.13, p=0.052). Similarly, in both age groups a notable increase in risk of underweight was observed. The risk of underweight increased significantly among residents of urban areas in 2014 by 3.38 (95% CI: 1.88-6.06, p<0.001) times more compared to year 2013 while in the rural areas the increased risk of underweight was not significant. There was no significant reduction in the prevalence of underweight among participants with helminth infections (*S. haematobium, S. mansoni* and hookworms) from 2013 to 2014 as shown in table 4.4b

Table 4.4b: Underweight with helminth infection, sex and age: Comparison of 2013 and 2014

Indicator	Number examined	% positives (Year 2013)	Number examined	% positives (Year 2014)	Odds ratio	95% CI*	P value
overall	748	100 (13.4)	771	143 (18.6)	1.47	1.11 to 1.95	p=0.006
Sex							
female	379	44 (11.6)	398	66 (16.6)	1.51	1.00 to 2.28	p=0.047
male	369	56 (15.2)	373	87 (20.6)	1.45	0.99 to 2.13	p=0.052
Age							
5 to 10 years	333	25 (7.5)	584	86 (14.7)	2.13	1.33 to 3.41	p=0.0013
11 to 17 years	415	75 (18.1)	187	57 (30.5)	1.99	1.33 to 2.98	p=0.0007
Areas							
urban	346	16 (4.6)	391	55 (14.1)	3.38	1.88 to 6.06	p<0.001
rural	402	84 (20.9)	380	88 (23.2)	1.14	0.81 to 1.60	p=0.445
S. haematobium							
negative	675	83 (12.3)	751	140 (18.6)	1.63	1.21 to 2.19	p<0.001
positive	73	17 (23.0)	20	3 (15.0)	0.58	0.15 to 2.25	p=0.427
S. mansoni							
negative	737	96 (13.0)	767	142 (18.5)	1.52	1.14 to 2.01	p=0.004
Positive	11	4 (36.4)	4	1 (25.0)	0.58	0.04 to 8.51	p=0.69
Hookworm							
negative	727	93 (12.8)	754	141 (18.7)	1.57	1.18 to 2.09	p=0.002
positive	21	7 (33.3)	17	2 (11.8)	0.27	0.04 to 1.64	p=0.12

4.5.3. Anaemia before and after MDA

Table 4.5c shows the distribution of anaemia by study variables across the two surveys. The overall prevalence of anaemia was 21.4% and 34.6% in 2013 and 2014 respectively (p<0.001). A 2.9 (95% CI: 1.96-4.19, p<0.0001) times increase in the risk of being anaemic was seen among female participants comparing year 2013 and 2014, significant. For male participants the increase in anemia was 1.3 times, and with that not significant (p=0.05). An analysis of the age groups indicated the risk of being anaemic significantly increased for the younger 5-10 year olds as well as for the 11 till 17 year olds. The analysis of the residential areas showed a divergent trend. There was a significant increased risk of anemia in rural areas from 2013 to 2014 by 6 times (95% CI: 4.07-8.06, p<0.001) while in urban areas the prevalence of anaemia reduced significantly by 47 % (95% CI: 17-67%, p=0.005) times. For the helminths it was seen, that for *S. mansoni* the infected and uninfected group showed similar increase in risk, but for *S. haematobium* and Hookworm the infected individuals showed a more dominant change. Table 4.4c.

Table 4.4c: Anaemia with helminth infection, malaria, sex and age: Comparison of 2013 and 2014

	year 2013		year 2014				
Variables	**Number examined**	**Positive (%)**	**Number examined**	**Positive (%)**	**Odds ratio**	**95% CI***	**P value**
overall	749	160 (21.4)	526	182 (34.6)	1.95	1.51 to 2.51	p<0.001
Sex							
female	380	59 (15.5)	284	98 (34.5)	2.87	1.96 to 4.19	p<0.0001
male	369	101 (27.4)	242	84 (34.7)	1.41	0.99 to 2.00	p=0.054
Age							
5 to 10 years	333	49 (14.7)	409	138 (33.7)	2.95	2.03 to 4.30	p<0.001
10 to 17 years	416	111 (26.7)	117	44 (37.46)	1.66	1.06 to 2.39	p=0.022
Areas							
Urban	346	65 (18.8)	295	32 (10.9)	0.43	0.29 to 0.83	P<0.001
Rural	403	95 (23.6)	231	150 (64.9)	6	4.07 to 8.86	p<0.001
S. haematobium							
Negative	676	137 (20.3)	511	171 (33.5)	1.98	1.52 to 2.58	p<0.001
Positive	73	23 (31.5)	15	11 (73.3)	5.98	1.59 to 22.5	p=0.003
S. mansoni							
Negative	738	156 (21.1)	522	180 (34.5)	1.96	1.52 to 2.54	p<0.001
Positive	11	4 (36.4)	4	2 (50.0)	1.75	0.16 to 19.54	p=0.645
Hookworm							
negative	728	152 (20.9)	516	174 (33.7)	1.93	1.49 to 2.50	p<0.001
Positive	21	8 (38.1)	10	8 (80.0)	6.5	0.91 to 46.58	p=0.032
Malaria							
negative	740	156(21.1)	481	140(29.1)	1.54	1.18 to 2.00	p<0.001
Positive	9	4(44.4)	45	42(93.3)	17.5	2.20 to 138.7	p<0.001

4.6. Association between helminth infections with Nutritional status and Anaemia

4.6.1. Association of Stunting with sex, age, area and helminth infections

Overall, among 1519 participants tested, 283 (18.6 %) were stunted. Of the 781, females were 121 (15. 5%) and 162of the 738 males (21.9%), p=0.01 were stunted. Adolescents aged 11-17 years were 3.4 (95% CI; 2.5-4.4-.p<0.001) times more likely to be stunted than those aged 5-10 years Rural participants were 1.4(95% CI; 1.0-1.4-.p=0.02) times more stunted compared to urban participants. Regarding helminth infections, no association of stunting was found for *S.haematobium* while for *S.mansoni* and hookworm infected participants both were 2.8 times more at risk of being stunted. Multilevel logistic regression analysis with districts of survey as random effect revealed that the risk of being stunted was 2.3 (95%CI; 1.1-4.6, p=0.03) times among participants infected with hookworms adjusted by year of survey, sex, age and area of residence (rural or urban). In contrast, it was observed that the risk of being stunted was not associated with schistosomiasis. Participants aged 11-17 years were 3 (96% CI; 2.3-4.0, p<0.001) times more at risk of being stunted adjusted by area, year of survey and infection table 4.5a.

Table 4.5a. Association of Stunting with age, sex, areas years and helminth infections

Variable		**Total Number examined =1516**	Univariate		Multivariate	
			Odd Ratio(95% CI)	P-value	Odd Ratio(95% CI)	P-value
Age (yrs)	5-10 yrs	915				
	11-17 yrs	601	3.4(2.5-4.4)	p<0.001	3.0 (2.3-4.0)	p<0.001
Sex	Female	780				
	Male	736	1.5(1.2-1.9)	p<0.001	1.3(0.9-1.7)	p=0.08
areas	Urban	738				
	Rural	778	1.4(1.04-1.8)	p=0.02	1.3(0.9-2.1)	P=0.20
years	2013	746				
	2014	770	0.47(0.37-0.60)	P<0.001	0.8(0.6-1.1)	0.3
S. haematobium	Negative	1424				
	Positive	92	1.3(0.8.2.2)	P=0.3	0.8(0.5-1.4)	0.4
S. mansoni	Negative	1503				
	Positive	13	2.8(0.9-8.6)	P=0.059	1.5(0.5-5.1)	0.5
Hookworms	Negative	1479				
	Positive	37	2.8(1.4-5.5)	P=0.002	2.3(1.1-4.6)	0.03

4.6.2. Association of underweight with age, sex, areas and helminth infections

The overall prevalence of underweight was 243(16.0%) out of 1519 participants. Females were 110 (14.2%) while males were 133 (17.9%). There was a significant difference in prevalence between the two analyzed 2 age groups; those 11-17 years old was 2.0 (95% CI: 1.5-2.7, p<001) times more likely to be underweight compared to those aged 5-10 years old, The prevalence of underweight was highly associated with area of residence whereas; those living in rural areas being 2.6 (95% CI: 2.0-3.6, p<0.001) times more likely to be stunted. There was no significant association between underweight and all the three infections in univariate and multivariate analysis. Multilevel logistic regression analysis with districts of survey as random effect revealed that the risk of being

underweight was 2.6 (95%CI; 1.9-3.5, p=0<0.01) times more in those aged 11-17 years old and 2.7 (95%CI , 2.0-3.6) times more in rural areas and 2.1(95%CI, 1.5-2.9,p<0.001) times more in 2014 adjusted by year of survey, sex, age and area of residence (rural or urban).Table 4.5b.

Table 4.5b: Associations of Underweight with sex, age area and helminth infection

Variable		Number examined =1519	Univariate		Multivariate	
			Odd Ratio(95% CI)	P-value	Odd Ratio(95% CI)	P-value
Age (yrs)	5-10 yrs	917	1.0			
	11-17 yrs	602	2.0(1.5-2.7)	p<0.001	2.6(1.9-3.5)	p<0.001
Sex	Female	777	1.0			
	Male	742	1.3(1.0-1.7)	P=0.046		
Areas	urban	737	1.0			
	Rural	782	2.6(2.0-3.6)	p<0.001	2.7(.2.0-3.6)	p<0.001
Years	2013	748	1.0			
	2014	771	1.5(1.1-1.9)	p=0.006	2.1 (1.5-2.9)	p<0.001
S. haematobium	Negative	1426	1.0			
	Positive	93	1.5 (0.9-2.5)	p=0.137		
S. mansoni	Negative	1504	1.0			
	Positive	15	2.7(0.9-7.9)	p=0.077		
Hookworms	Negative	1481	1.0			
	Positive	38	1.7(0.8-3.5)	p=0.19		

4.6.3. Association of Anaemia with age, sex, areas, helminth infections and Malaria

Out of 1275 participants examined 342 (26.8%) were anaemic. Males were 1.4 (95% CI; 1.1-1.8, p<0.008) times more likely to be anaemic than females. Rural areas participants were 3.5(95% CI; 2.7-3.7, p<0.001) and 1.9(95% CI, 1.5-2.5) times more in year 2014. Moreover, participants infected with *S. haematobium* were 1.8 (95% CI: 1.2-2.8 p=0.009) times more at risk of being anaemia than those non- infected. A notable non-significant association between anaemia and *S. mansoni* and hook infection prevalence was observed. Malaria infected individuals were 18 (95% CI, 8.9-39.7, p<0.001) times more at risk of being anaemic compared to those with no malaria infected participants.

The major impact on anaemia was seen through malaria. There was an increase in malaria cases from 2013 to 2014. As a result there was a rise in prevalence of anemia in the respective area.

Individuals infected with plasmodia were found to be 7.8 times more likely to be anaemic. Overall, after adjusting for age, area of residence, sex and nutritional status the risk of being anaemic was 2.4 (95% CI; 1.8-3.2, p<0.001) times more in year 2014 compared to year 2013. The risk of being anaemic was higher among rural participants by 3.5(95% CI; 2.5-4.5, p<0.001) times compared to urban participants adjusted by age, sex, year of survey and nutritional status. Moreover males were 1.4 (95%CI; 1.1-1.9-2, p=0.012) times anaemic in a multivariate analysis adjusted by other variables as shown in the t*able 4.5c*.

Table 4.5c: Association between anaemic with sex, age area year, helminth infections and Malaria

Variable		Total Number examined =1275	Univariate		Multivariate	
			Odd Ratio(95% CI)	P-value	Odd Ratio(95% CI)	P-value
Age (yrs)	5-10 yrs	742	1.0			
	11-17 yrs	533	1.2(0.9-1.6)	p=0.12	1.5(1.2 -2.1)	p=0.004
Sex	Female	664	1.0			
	Male	611	1.4(1.1-1.8)	p=0.0076	1.4(1.1-.1.9	p=0.012
Areas	Urban	641	1.0			
	Rural	634	3.5(2.7-4.7)	p<0.001	3.4(2.5-4.5)	p<0.001
Years	2013	749	1.0			
	2014	526	1.9(1.5-2.5)	p<0.001	2.4(1.8-3.2)	p<0.001
S. haematobium	Negative	1,187	1.0			
	Positive	88	1.8(.1.2-2.8)	0.009		
S. mansoni	Negative	1,260	1.0			
	Positive	15	1.8(0.6-5.2)	0.24		
Hookworm	Negative	1244	1.0			
	Positive	31	3.0(1.5-6.2)	p=0.0016		
Malaria	Negative	1221	1.0			
	Positive	54	18(8.9-39.7)	p<0.001	7.8(3.5-17.1)	p<0.001

4.7. Multiple helminth infections profiles by years of surveys

The infection profile with helminthiases involved parasitological examination of 749 participants aged 5 to 17 years old in 2013 and 743 in 2014. The infection profile for 2013 was as follows: participants with single helminth infections were 90 (12.0%); double infections were 8 (1%) while only 1 (0.7%) participant was found with triple infections. Single infections found were *S. haematobium* 68 (8.7%), *S. mansoni* 8 (1.1%), hookworms 13 (1.7%) and LF 4 (0.5%). Double

infections were of three combinations; S. haematobium and *S. mansoni*; *S. haematobium* and hookworm and *S. mansoni* and hookworm. The distribution is as shown in the table 4.6.

In the 2014 survey, the helminthes infection profiles were single 38 (5.1%) and double were 3 (0.4%). There were no triple infections observed. A notable crude reduction of single infected participants by 60.1% (95% CI; 41.3%-73.5%, p<0.001) in year 2014 compared to 2013 was observed. For double infections a non-significant crude reduction was observed. Participants infected with at least one of helminthiases among LF, hookworm, S. mansoni and *S. haematobium* herein referred to as *"any infection"* in the 2013 survey a higher prevalence 99 (13.2%) compared to the prevalence of at least one infection 41 (5.5%) in year 2014, (p<0.001). The crude reduction rate of at least any infection in year 2014 was 61. 7% (95%CI; 43.8%-73.8%, p<0.001).

Table 4.6: Helminths infection profiles by year of survey (before and after MDA)

	Year 2013	**Year 2014**
Variables	**Prevalence (n=749)**	**Prevalence (n=743)**
None	650 (86.8)	702 (94,5)
single	90 (12.0)	38 (5.1)
Double	8 (1.0)	3 (o.4)
Triple	1 (0.1)	0 (0.0)
Diseases profiles		
None	650 (86.8)	702 (94,5)
S. haematobium	68 (8.7)	17 (2.3)
S. mansoni	8 (1.1)	3 (0.4)
Hookworm	13 (1.7)	14 (1.9)
LF	4 (0.5)	4(0.5)
S. *haematobium + S. mansoni*	1(0.1)	0(0.0)
S. haematobium + Hookworm	6 (0.8)	2 (0.3)
S. mansoni + Hookworm	1(0.1)	1 (0.1)
S. haematobium + *S. mansoni* +Hookworm	1 (0.1)	0 (0.0)
Any infection	99 (13.2)	41 (5.5)

4.8. Correlation of "any infection" with nutritional status and anaemia

The proportion of helminth infection on nutritional markers was analyzed for both years.

In 2013, 165 individuals were defined as stunted and 27 (16.4%) of them suffered from a helminth infection. In 2014 this dropped to 9/105 (8.6%), showing a non-significant crude change, p<0.07.

Proportion of underweight among participants with any infection was 24/100 (24.0 %) in 2013 and significantly dropped to 6/135 (4.4%) in 2014 (p<0.001). For anaemia findings indicated that the prevalence of participants with any infection and anaemic was 33/160 (20.6%) in 2013, and significant reduced to 22/174 (12.6%), p=0.05.

When adjusting for sex, age, stunting, anaemia year of survey and taking district as random effect in the model; the prevalence of participants with any infection, significantly reduced by 63% (95% CI: 36%-78%, p<0.001) in year 2014 compared to 2013. Moreover, anaemia increased by 1.7 (95%CI: 1.1-2.7, p=0.018) times in those participants with "any infection" helminth infections adjusted by year of survey, sex, nutritional status and anaemia as shown in *table 4.8*.

Table 4.7: Relationship between "any infection" and other co variables (adjusted)

Type	Variable	No. examined	Odds ratio	95% CI	p_value
Year of Survey	2013	746	1		
	2014	457	0.37	0.22-0.64	p<0.001
Sex	Female	625	1		
	Male	578	1.3	0.98 -1.99	P=0.16
Age group	5-10 years	679	1		
	11--17 years	524	1.48	0.97-2.28	0.07
Stunted	Normal	964	1		
	Stunted	239	1	0.62-1.62	p=0.99
Anaemia	Normal	876	1		
	Anaemic	327	1.72	1.10-2.71	p=0.018
Malaria	Negative	1152	1		
	Positive	51	1.5	0.69-3.26	P=0.31

4.9. Helminth and atopic diseases

Dust mites' allergens (*D.farinae* and D. *pteronyssinus)* and cockroach allergens *(Blatella germanica)* were used for Skin Prick Test (SPT) only in year 2014. The assessment was on individuals aged 5-17 years old.

780 participants were tested for all the 3 allergens. Forty one 38/780 (4.9%) of participants tested positive for D. farinae allergen. More participants aged 11-17 years 16/192 (8.3%) reacted positively against *D. farinae* than those aged 5 to 10 years 22/588 (3.7%), p=0.01. Likewise more participants from rural areas 31/387 (8. 0%) than urban 7/393 (1.8%) reacted positively against this allergen

(p<0.001). Furthermore, unadjusted to other confounding variables, our findings indicate that, people in rural areas were 4.8 (95% CI; 2.1 -11.1, p<0.001) times more of being reactive to *D. farinae*. Using a random effects logistic regression analysis, it was noted that those participants from ages 11-17 years old were 2.0(95%CI; 1.0-3.9, p, 0.04) times more reactive to dust mites than younger ones and rural areas ones were 4.5 (95%CI; 1.9-10.4, p=0.001) times more reactive to *D. farinae* compared to those from urban areas adjusted by the effect of infections, sex and age. Only hookworm infected participants were 4.5 times more infected than those without infection (p=0.0134).

Table 4. 8a: Associations of between D farinae atopy and age, sex, areas and helminth infections

Variable		Total Number examined =780	Univariate		Multivariate	
			Odd Ratio(95% CI)	P-value	Odd Ratio(95% CI)	P-value
Age (yrs)	5-10 yrs	588	1.0			
	11-17 yrs	192	2.3(1.9-4.6)	p=0.01	2.0(1.0-3.9)	p=0.04
Sex	Female	405	1.0			
	Male	375	0.6(0.3-1.2)	p=0.1		
areas	Urban	393	1.0			
	Rural	387	4.8(2.1-11.1)	p=0.0001	4.5(1.9-10.4)	p<0.001
S. haematobium	Negative	760	1.0			
	Positive	20	2.2(0.5-10.0)	p=0.3		
S. mansoni	Negative	776	1.0			
	Positive	4	6.7(0.7-65.0)	p=0.06		
Hookworms	Negative	763	1.0			
	Positive	17	4.5(1.2-16.3)	p=0.0134		

Overall 31/780 (3.9%) participants reacted positive for *D. pteronyssinus*. More female participants 23/405 (5.7%) reacted compared to males 8/375 (2.1%), p=0.01. Participants aged 11-17 years old 12/192 (6.3%) were more reactive against this allergen and participants from rural areas 25/387 (6.5%) were more reactive than in urban areas 6 /393 (1.5%), p<0001. Multivariate analysis, indicated that the risk of reacting against *D. pteronyssinus* was 8.4 (95%CI; 2.5-27.8), p<0.001) times among participants infected with hookworm compared to those without hookworm infection. Males were 60% (95%CI; 20% -80%, p=0.01) less of being reactive against *D. pteronyssinus* compared to females .After adjusting for age, infections and sex rural areas were 60% (95% CI,30%-90%) less

prone to react for *D. pteronyssinu*s.. Likewise rural areas and hookworm infected participants were 4(1.6-10.1, p=0,003 and 5.8 (1.7-20-3) times more prone respectively to react against this atopy.

Table 4.8b Associations between D. pteronyssinus atopy and age, sex, areas and helminth infections

Variable		Total Number examined =780	Univariate		Multivariate	
			Odd Ratio (95% CI)	P-value	Odd Ratio(95% CI)	P-value
Age (yrs)	5-10 yrs	588	1.0			
	11-17 yrs	192	2.0(0.9-4.2)	p=0.06	0.4(0.1-0.7)	0.011
Sex	Female	405	1.0			
	Male	375	0.4(0.2-0.8)	p=0.01		
areas	urban	393	1.0			
	rural	387	4.5(1.8-11.1)	p=.0004	4.0(1.6-10.1)	p=0.003
S. haematobium	Negative	760	1.0			
	Positive	20	1.3(0.2-9.9)	p=0.8		
Hookworms	Negative	763	1.0			
	Positive	17	8.4(2.5-27.8)	p<0.001	5.8(1.7-20.3)	p=0.005

A total 56/780(7.2%) tested positive for cockroach allergen and contrary to the 2 previous SPT tests above, significantly more 41/393(10.4%) participants from urban areas than rural 15/387 (3.8%) (p<0.001).

However our findings revealed that there was no significant association of *S. mansoni, S. haematobium* infection for that allergen as shown in (table 4.8c). None of the helminth infections showed an association with the skin prick test for *Blatella germanica* (cockroach).

Table4.8c: Associations between cockroach atopy and age, sex, areas and helminth infections

Variable		Total Number examined =780	Univariate		Multivariate	
			Odd Ratio(95% CI)	P-value	Odd Ratio(95% CI)	P-value
Age (yrs)	5-10 yrs	588	1.0			
	11-17 yrs	192	1.8(1.0-3.2)	p=0.05		
Sex	Female	405	1.0			
	Male	375	0.7(0.4-1.2)	p=0.2		
areas	urban	393	1.0			
	rural	387	0.4(0.2-0.6)	p=0.0004	0.4(0.2-0.6)	p=0.001
S. haematobium	Negative	760	1.0			
	Positive	20	0.7(0.1-5.1)	p=0.7		
Hookworms	Negative	763	1.0			
	Positive	17	1.8(0.4-7.9)	p=0.5		

5. Discussion

5.1. General Burden and MDA for NTDS

Helminth infections are among the NTDs which pose a threat to the health and socio-economic wellbeing of populations in endemic communities, with an estimated 1.7 billion people globally at risk of at least 1 NTD. The 17 NTDs described by WHO are infectious diseases, caused by viruses, fungi, bacteria and helminths. NTDs can be prevented, or even eliminated, with a simple, safe and effective intervention known preventive chemotherapy or mass drug administration (MDA). This fact has brought together policy makers and experts in the field of NTDs control to commit resources for their control and eventual elimination. Endemic countries have established control and elimination programmes and instituted treatment campaigns for that effect. Tanzania is endemic for helminthic infections and the entire population is at risk for at least 1 of the diseases among schistosomiases and STH (*T. trichiura, A. lumbricoides* and hookworm) with children and adults living in poverty being most vulnerable to infections. The country has adopted the WHO resolutions to eliminate or control NTDs and has since 2009 established the Neglected Tropical diseases control programme (NTDCP) to integrate control of NTDs including the helminth infections which were formerly controlled through disease specific control programmes. Recently (2013) a comprehensive resolution for 17 NTDs was adopted. The programme is operational countrywide where by MDA activities are conducted with respective endemic diseases and are organized at the district level. As school age children are affected most by STH and schistosomiasis, they are specifically targeted for control using albendazole and praziquantel at least once yearly [91-93]. For LF elimination the target is to those aged 5 years old and above and the drugs of choice are ivermectin and albendazole, because for LF a different age distribution was reported with low prevalence in children. The current study aimed at elucidating the helminth disease burden and its association before commencement of MDA and after at least one round of intervention. The purpose was to inform policy decisions.

5.2. Methodological issues

Our study focused on helminth infections and the mass drug administration specifically for helminth infections. Using the cross sectional design, data was collected to provide a snapshot of the magnitude and intensity of helminth infections and their associations with selected health indicators in the study communities before and after the commencement of MDA. The cross-

sectional studies have been extensively used for community based disease control monitoring to facilitate the assessment of the burden of diseases and impact of intervention at the community level and therefore allow planning and allocation of resources for their control.

5.3. Data collection approaches and applications

The methods used in the study were appropriate according to WHO recommendations. For determining the prevalence of LF, ICT Binax NOW® was used. This point of care test is based on the detection of circulating filarial antigen and is used globally for in eradication programmes. For STH and SCH the Kato the direct detection of helminth eggs through Kato Katz technique has been used, as it was described by several field studies in Africa [84] to determine the prevalence and intensity of the schistosomiases and STH. Of late there exits other tests for Schistosomiasis nowadays including the Circulating Cathodic antigen CCA) used to determine antibody against *S .mansoni* in urine. This test more sensitive than Kato Katz and it is user friendly in the field settings [94]. Kato Katz was used because it cuts over for other helminths as well, not only *S. mansoni* and hence it was cost effective. Moreover other serological tests were expensive and required specialized skills and equipment.

The nutritional status was determined by using anthropometric measurements of height in centimeters and weight in kilogram by using a ruler and weighing scale respectively. For the relationship between allergies and helminths, skin prick test was determined by using a standardized HAL products (dust mites-*D. farinae, D. pteronyssinus*) droppers and lancets and cockroach (*Blatella germanica*) products were used. The procedure is extensively applied due to its safe and cost –effectiveness. Other laboratory tests like blood tests takes long and are less sensitive than SPT[95]. Analysis of data was appropriate using STATA version 12.

5.4. Role of research in NTD programmes and MOH

The NTDCP is an intervention programme of public health under the Ministry of Health, Community Development, Gender, Elderly and Children which conducts its activities under the coordination of the Directorate of Preventive Services. The programme mandates include coordination of the implementation of interventions related to control and elimination of NTDs. The monitoring and evaluation as well as operational research which aim to inform the programme about what works better and where to improve form an important component of programme activities. This is done in

collaboration with research institutes. Being part of the NTD programme and my involvement in monitoring and evaluation (M&E) activities for the past 10 years, I have gained experience and skills in formulating operational research agenda to inform the daily implementation issues of the programme. The knowledge and experience acquired enabled me to critically analyze performance data gathered by the programme staff and select the study sites in accordance to preliminary mapping results. In addition, it enabled me to conceive the research idea, generate the research questions and thus design this study.

I developed the ideas of this thesis myself and I aimed to generate evidence of prevalence and intensity of PCT targeted helminths infections, its associated health indicators and impact of PCT. I also hoped to fill in the gap on contradictory findings on relationship between helminth infections with atopy, which are not addressed in governmental programmes, but require research interest. Because of the limited time for the PhD field work, after applying for and receiving ethical approval, and leaving time for analysis, the impact of MDA on helminth and its associated indicators was assessed prior and after only one round of MDA.

5.5. Discussion of the results

5.5.1. The prevalence of NTDs and helminths

This study has shown predominance of infections with *S. haematobium*. Although there were considerable reductions in all infections after one round of Preventive Chemotherapy (PCT) the infections with *S. haematobium* still persisted especially in the rural areas. Similar findings of *S.haematobium* predominance have been reported in the review done in Sub- Saharan Africa which indicated a larger populations suffering from complications related to infections of *S. haematobium* than those with *S. mansoni* [7, 96, 97]. The results reported by Lwambo *et al*., indicted the spreading of *S. mansoni* in areas close to Lake Victoria while *S. haematobium* being evenly distributed elsewhere [76].

Among the STH, this study has shown the dominance of hookworm infections compared to other worms. Previous studies conducted in Tanzania and other Sub-Saharan Africa countries have reported same hookworm dominance among helminthiases [7].

There was neither *T. trichiura* nor *A. lumbricoides* infections in the four chosen survey areas. Lwambo et al. in 1999 also found rare Trichuris and Ascaris infections in Tanzania [76]. Recent publications

from Southwest Tanzania described areas with *T. trichiura* and *A. lumbricoides*; however lower prevalence compared with hookworm infections and patchy distribution was shown [98, 99]. Contrary to our findings, studies in Congo and West Africa reported predominance of *T. trichiura* and *A. lumbricoides* infections [100, 101] in comparison with other worms. The variability in species prevalence is due to geospatial and ecological factors including water resources and development management [76, 99, 102, 103]. Emerging findings are consistent with that of *Mabaso et al. (2004),* which showed the linkage between hookworm and soil porosity, whereby, sandy soil was reported to be favorable for hookworm development [104].

5.5.2. Helminth infections prevalence burden level

Helminths infections still pose a big challenge to public health and socio-economic wellbeing of endemic communities. During baseline survey in year 2013, prevalence of LF, *S. haematobium, S. mansoni* and hookworm was lower in both rural and urban districts in comparison with preliminary studies of the governmental NTD control programme [70] which indicated estimated prevalence of < 6 % for LF and 23% to 38% for *S. haematobium* in Mwanza districts. For Dar es Salaam, estimates from NTDCP indicated that LF prevalence in Temeke district ranged from 8% to 36%, and Kinondoni from 21% to 38% while for schistosomiasis the range of infection across the region ranged from 10% to 15% in the sentinel sites. A review of schistosomiases by Mazigo et al. in 2012 also indicated a much higher prevalence compared to our findings [105]. There has been limited or no district wide MDA has been a challenge in the study areas though the national programme had been treating most of the coastal and inland districts. One round of school based MDA was done in 2005 in Mwanza by the National Schistosomiasis Control Programme (NSCCP) whereby school aged children were treated with praziquantel and albendazole in both Dar es Salaam and Mwanza districts. In the Dar es Salaam region (urban areas) community members aged 5 years and above received 2 rounds of MDA in year 2006 and 2007 using ivermectin and albendazole for LF elimination. Due to unavoidable reasons no more MDA rounds were conducted in the Dar and Mwanza since 2007. Baseline data collection for this study was done in 2013, prior to MDA conducted by the national programme. This was the district wide MDA with praziquantel and albendazole in all primary schools in Mwanza. In Dar es Salaam districtwide ivermectin and albendazole MDA was administered to all people above 5 years and praziquantel only to school aged children (5 to 17 years of age). Despite

many obstacles and interrupted MDA activities, the helminth prevalence found in year 2013, the baseline survey for my studies, were much lower, than generally expected. Impact data was collected 12-14 months after MDA and was in 2014.

This study found no case of schistosomiases, 1 case of hookworm and no other STH in the urban areas. Positive cases for all helminth infections were only found in rural areas. *T. trichiura* and *A. lumbricoides* and hookworms are sensitive to treatment with albendazole, so the LF treatments in Dar es Salaam, using ivermectin and albendazole might have had an overlapping effect on the prevalence of STH. These findings were supported by Massa *et al*., who reported the combined effects of LF treatment on STH. [106]. In addition, emerging findings seem to be consistent with findings from a recent study conducted in Dar Es-Salaam and Tanga regions which also showed less than 1% STH and SCH prevalence [107]. Prevalence of LF was higher in urban than rural areas as reported in several other studies. The urban areas in this study were the coastal areas. Several studies have noted same dominance of disease in coastal areas compared to inlands [53, 108, 109].

5.5.3. Helminth infections and gender

In the survey, male individuals were more prone to *S. haematobium* than females. Similar findings were observed in a study conducted a decade ago in Kinondoni district, Dar es Salaam region [110] and in Ethiopia [111]. But for the case of *S. mansoni*, results from the survey showed no gender difference among school aged children; a finding similar to a study conducted in Mwanza [112, 113]. The observed increased risk in males for schistosomiasis could be due to the social economic activities among males, for example, fishing activities. For LF, however, no gender difference was noted which correlates to recent findings in Dar es-salaam and Tanga regions [114, 115]. Nevertheless these findings are contrary to studies conducted in Tanzania, Congo and Nigeria which indicated male dominance in prevalence of LF infection, but only for individuals above 18 years of age [109, 116, 117].

5.5.4. Helminth infections and age

This study has indicated a significantly higher prevalence of *S. haematobium* among children aged 11-17 years old than their younger counterparts. This may be attributed to the fact that the older group are more likely to play in water bodies and thereby be exposed to breeding sites for the

disease causing pathogens. For hookworm no significant trend was noted between younger and older children [91, 92].

A notable trend in prevalence of LF increase with age was observed at baseline in 2013. This correlated with findings from a study done in Tanga which is also a coastal region like Dar es Salaam (both regions are in Tanzania) [61, 118]. However after 1 round of MDA the CFA prevalence of the infection seemed to decrease but remained high in participants aged 18-24 years old. These finding might be attributed to low MDA compliance especially for urban communities due to diverse activities and reluctance on MDA as a community based activity. This same low compliance for urban communities is noted in a study by *Ramaiah et al., [119].*

5.5.5. Multiple helminth infections

Studies in Mwanza and Pemba indicated existence of coexistence multiple helminth infections in one individual [73, 120]. Our findings also indicate that most co-infections were either hookworm and *S. haematobium* or hookworm and *S. mansoni*. However, in another study conducted earlier in Mwanza region, Lwambo et al. (1999), found that hookworm and *S. mansoni* co-infections occurred more frequently as multiple infections than as single species infection [76]. It was planned to investigate the role of polyparasitism on stunting, underweight and anaemia. However, only few individuals had more than one parasite, hence, this analysis could not be performed.

5.5.6. Helminth & nutritional Status

The study also evaluated the association between helminth infections and some important health indicators such as nutritional status (stunting, underweight), anaemia and allergies.

Among the 3 helminth infections, stunting was significantly associated with only hookworm infection (crude and adjusted). Findings from Uganda indicated also the relationship of *S. mansoni* with stunting [121]. These findings are consistent with findings by Lwambo and *Lwanga et al.* [122-124]. Our study showed a non- significant 1.5 times increased risk of stunting in participants infected with *S. mansoni*. However, because of small numbers of infection in my study, this finding remained a trend, but remains concordant with the findings from Lwambo and Lwanga.

Underweight was positively associated with the infection of both Schistosoma species and also hookworm in the crude analysis. However, after adjustment for age, gender and area, no significant

influence of helminth infections in underweight was seen anymore. This finding is supported by a study from Ethiopia indicating no association of STH and nutritional status [125].

5.5.7. Anaemia general

Prevalence of anaemia reported in this study in 2013 was 22.7% which is comparable to the Tanzania HIV& Malaria indicator Survey (THMIS) which reported a prevalence of 19% for Mwanza region in year 2012 [126]. However, the prevalence was low as compared to that recorded in other studies of school children in Tanzania. Studies done by Kinunghi and Lwambo showed prevalence of anaemia to be 34% and 62.6% respectively in the same region of Mwanza [122, 127] while Hall et al. reported a prevalence of 52% in Lake zone [128]. In Tanga Region, Tatala et.al. reported anaemia prevalence of 79.6% which was higher than the previous studies [129]. The relatively low anaemia observed in the present study may be attributed to the low helminths infection prevalence and intensities with less coinfections in the study communities.

This study indicated that participants aged 11-17 years old were 1.5 times more at risk for anaemia compared to younger children. This observation is largely explained by the higher prevalence of anaemia among 11-17 years olds compared to 5-10years olds at baseline in 2013. However, these findings are interesting as they are in contrast with earlier studies which showed an inverse relationship between prevalence of anaemia with age among school age children as reported in Tanzania by *Lwambo et al* and by Mupfasoni et al., in Rwanda [122, 124]. The increase in anaemia with age may be explained by correlation of age with stunting, underweight and also malaria as we noted same trend in all mentioned aspects.

5.5.7.1. Helminths and anaemia

Prevalence of anaemia was significant associated with all helminth infections with the exception of *S.mansoni*, This association is also found in other studies conducted elsewhere [122, 130, 131]. Likewise the present study indicated that individuals with “any infection” were 1.7 times more at risk of being anaemic (adjusted). Another study in Uganda indicated that heavily *S. mansoni* and hookworm infected children had low haemoglobin levels and improved after praziquantel and

albendazole treatment [17]. Contrary ,a study in Rwanda reported neither association of helminth and anemia nor helminth with stunting [132].

5.5.7.2. Anaemia and malaria

Evaluation of anaemia before and after helminth treatment was conducted in areas where malaria is also prevalent. There were more cases of malaria in year 2014 compared with 2013 and this largely explains the increase of anaemia in year 2014. This was unexpected and affected the investigation of the effects of helminth treatment on anaemia. In the rural areas prevalence of anaemia increased by 6 times in 2014 compared to 2013. This increase correlated to increase in malaria incidence prevalence in both Sengerema and Kwimba in 2014 compared to 2013 (THMIS unpublished data). Low coverage of malaria prevention interventions can result in increased malaria burden. In 2014, indoor residual spraying (IRS) was not done in both Kwimba and Sengerema districts unlike 2013 when IRS was done in Sengerema. In addition, it can be expected that by 2014 community coverage with long lasting insecticidal nets (LLINs) may have decreased considerably following net attrition since the mass net distribution campaign in 2011. Malaria transmission is throughout the year but is increased during the rainy season. For Dar es Salaam (urban areas) surveys were collected almost during same seasons. Therefore, the effect is well compared while for rural areas (Mwanza) there was a difference between baseline (July) and impact time (September-October) and this might be associated with infection peak season. As a result, data collection timings could be a contributing factor for the difference in malaria prevalence observed especially in rural areas between years of surveys.

The results from the two surveys indicated that after 1 round of MDA there was a crude reduction in anaemia by 47% in urban areas. Findings also noted less participants infected with malaria were from urban areas compared to rural areas. The results of low prevalence in the urban districts are supported by previous surveys in 2011 [126]. This might be explained by increased awareness on mosquito control and use of bed nets in urban areas. Similar findings of low urban malaria prevalence was noted in a study conducted in Tanga city in year 2007 [133].

5.5.8. Helminths & allergy surrogate marker

In the survey more skin prick positive individuals were found in rural areas than in urban areas. This is in contrast to previous findings by Cooper et al., [30], though newer publications have similar findings. For example, writing in 2006, Bloomfield questioned whether it would be time to abandon the hygiene hypothesis [134]. Webb et al., found helminths positively associated with atopy [135]. In the present study, more helminth were found in rural areas and participants from rural areas (adjusted) were 4.8 and 4.5 times more at risk of being reactive for *D. farinae* and D. *pteronyssinus* allergens respectively than in participants from urban areas; a finding similar to studies by Webb and Bloomfield. Again, this is in contrast to other findings whereby helminth infections were reported to be inversely related to allergies [36, 136, 137]. Emerging findings showed that the relationship between helminth infections and allergies was only among participants infected with hookworms, who were reactive to *D. farinae and D. pteronyssinus.* After adjusting for effect of sex, age, areas and other infections (*S. haematobium*) the risk of being reactive to *D. pteronyssinus* allergen remained significant and was 5.8 times more among hookworm infected participants compared to those not infected. A recent published study reported similar findings on direct relationship between atopy and helminths infections in Uganda [135]. Whether this indicates that hookworm promoted allergic reactions specifically with dust mites, or whether a cross reactivity of IgE might explain this results, needs further evaluation. For sensitization against cockroach a different pattern was found in our study, cockroaches are less found in rural areas and more in urban areas, which might be explained by environmental factors favoring them. Again, a recent study by Nyan et al also reported that the risk of being sensitized to a cockroach allergens less by 60% in rural areas [36]. In summary, my study cannot support the hygiene hypothesis by *D. Strachan* but is in agreement with recent publications challenging the concept [34, 134]. Unfortunately, a planned post treatment evaluation of skin prick test positivity could not be performed because of technical problem. Therefore, potential changes in skin prick positivity after helminth treatment cannot be reported.

5.6. *Helminths* infection prevalence reduction (impact of MDA)

In the year 2014, prevalence of all endemic helminths decreased. However, after adjusting for age, sex, anaemia and stunting, prevalence of *S. haematobium* infection decreased significantly by 74% and those who had single infections reduced significantly. Among participants with double and triple infection prevalence was also reduced. Similar findings of helminths infection prevalence reduction after several rounds of MDA were reported in several studies conducted in the country [114, 118, 124, 138]. Our findings also indicate a low *S. mansoni* prevalence and non-significant reduction after 1 round of MDA. *S. mansoni* and Hookworm infections significantly dropped after several rounds of comprehensive interventions including MDA and PHAST implemented in Kome Island [139]. Reduction of prevalence of participants with "any infection was 63% (adjusted) after (1) one of MDA. Therefore our findings suggest that even a single round of MDA may have an impact on helminth infection. The intensity of helminth infections specifically *S.mansoni* significantly decreased in the 2014 survey as compared to an earlier survey in 2013. There was neither heavy nor moderate infections categories of all the 3 helminths in year 2014. This trend in category reduction is also promoted and recommended by WHO.

The reduction of infection intensity after interventions has been noted in several other studies. For instance a study in Zanzibar by *Knopp et al* in 2010 indicated that several rounds of MDA treatment decreased helminth intensity although prevalence and anaemia remain unchanged [140].

6. CONCLUSION

This study shows several interesting results: At baseline the three helminth infections, hookworm, *S. mansoni* and *S. haematobium* showed a significant association with underweight in children, while hookworm and *S. haematobium* were also associated with stunting and anaemia. Rural areas were more affected with helminth infections than urban areas. One round of mass drug administration with appropriate anthelminthic drugs showed a significant reduction in prevalence for *S. haematobium* and a marked significant reduction for *S. mansoni* and hookworm intensity was demonstrated too. There was a significant reduction of prevalence of participants with single helminth infection as well as those with "*Any infection*" .Interestingly, after one round of MDA, a non-significant reduction of the stunted and helminth infected children and increased prevalence of anaemia was observed mostly in rural areas. The increase in anaemia is explained by malaria increase in 2014. Malaria is an acute life-threatening infection has a much more dramatic influence on blood parameters than helminth infections. As the malaria prevalence rose between 2013 and 2014 also supported by THMIS. An increase in anaemia was seen only in the rural areas of Mwanza. In contrast, in the coastal urban areas, a drop in anaemia was seen after helminth treatment, demonstrating the positive effect of the MDA activity. This demonstrates the challenge of cross sectional studies, which focus on a specific group of diseases. If information about additional diseases in the study area is not available, a change in prevalence of that other sickness can severely influence the outcome and lead to wrong interpretations. Despite solving this severe problem of potential confounding, this study had several additional limitations. For example, the overall prevalence of helminth infections in the chosen areas was much lower than expected, therefore, reducing the possible effects on outcome parameters and also effects of interventions. Another unfortunate limitation was the unavailability of the tests for allergic surrogate marker at baseline. As our results for 2014 were interesting and different to some of the previous reports, it would have added enormously to the interpretation to have results after helminth treatment.

Mainly schistosomiases and hookworm infections are still prevalent in Tanzania and rural areas are still more affected. A positive association between helminth infection prevalence/intensity and its impact indicators such as stunting, underweight, anaemia was observed. Although only 1 round of anthelminthic medicines PCT was administered, it offers hope for effective intervention against

helminth prevalence and intensity. Other diseases, like malaria occur in similar areas, and have to be taken into account, when evaluating the effect of MDA activities. Therefore PCT intervention needs to be promoted to gain multiple effects on helminths infection reduction and its associated health impact indicators.

6.1. Policy recommendations

The survey has revealed that after one round of MDA there was a considerable reduction in the prevalence and intensity of infection with helminthiases although they still pose health problem. We recommend that NTDCP continues with regular mass treatment according to the WHO guidelines for their eventual elimination as evidence from other countries has shown. This should be done hand in hand with regular monitoring and evaluation to detect any visible changes in the status of infection and intensity. The monitoring should target not only the presence of parasites, but other health indicators associated with helminth infections as well. The monitoring should also aim to inform on research needs of the programme.

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8. ANNEXES

8.1. Curriculum Vitae

Surname	MWINGIRA	First name(s)	UPENDO
Profession	Medical Doctor and Researcher	Job title	Senior Research Scientist-Programme Manager for Neglected Tropical Diseases Control programme
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Academic positions			
2012-todate	PhD student, University of Munich-German		
Education			
2006-2007	Masters of Tropical Medicine, University of Nagasaki-Japan		
1994-2000	Medical doctor-Russian Peoples Friendship University-Russia		

Professional Membership

2009 to date	Member of the American Society of Tropical Medicine and hygiene
2004 to date	Member of the Tanzania public Health Association
2004 to date	Member of the Tanzania Medical Association

8.2. List of Publications

- Heather N. Paulin, Andreas Nshala, Akili Kalinga, **Upendo Mwingira**, Ryan Wiegand, Vitaliano Cama, Paul T. Cantey. Evaluation of Onchocerciasis Transmission in Tanzania: Preliminary Rapid Field Results in the Tukuyu Focus, 2015.The American Journal of Tropical Medicine and Hygiene, Volume 97, Issue 3, Sep 2017, p. 673 - 676, DOI: https://doi.org/10.4269/ajtmh.16-0988
- Gass KM, Sime H, **Mwingira U.J**, Nshala A, Chikawe M, Pelletreau S, et al. (2017) The rationale and cost-effectiveness of a confirmatory mapping tool for lymphatic filariasis: Examples from Ethiopia and Tanzania. PLoS Negl Trop Dis 11 (10): e0005944. https://doi.org/10.1371/journal. pntd.0005944
- **Upendo J. Mwingira***, Philip Downs, Cecilia Uisso, Maria Chikawe, Matthieu Sauvage-Mar, Mwelecele N. Malecela, Kathryn Crowley, Jeremiah M. Ngondi. Applying a mobile survey tool for assessing lymphatic filariasis morbidity in Mtwara Municipal Council of Tanzania 15 March 2017. Mhealth A journal for research, validation and mobile technology digital health and Medicine http://mhealth.amegroups.com/article/view/13969/14227
- **Upendo J. Mwingira**, George Kabona, Mathias Kamugisha, Edward Kirumbi, Bernard Kilembe, Alistidia Simon, Andreas Nshala, Deogratias Damas, Alphonsina Nanai, Mwelecele Malecela, Maria Chikawe, Christina Mbise, Harran Mkocha, Patrick Massae, Humphrey R. Mkali, Lisa Rotondo, Kathryn Crowley, Rebecca Willis, Anthony W. Solomon & Jeremiah M. Ngondi (2016): Progress of Trachoma Mapping in Mainland Tanzania: Results of Baseline Surveys from 2012 to 2014, Ophthalmic Epidemiology, DOI:10.1080/09286586.2016.1236974 http://dx.doi.org/10.1080/09286586.2016.123697. Published with license by Taylor & Francis
- **Upendo Mwingira**, Arianna Rubin Means, Maria Chikawe, Bernard Kilembe Dafrossa Lyimo, Andreas Nshala, Alex Mphuru. Integrating Neglected Tropical Disease and Immunization Programs: The Experiences of the Tanzanian Ministry of Health. American Journal Of Tropical Medicine and Hyegine.May 2016
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Statement on press-release and contribution

The PhD thesis titled '*Evaluation of the health impact of integrated helminths control by preventive chemotherapy in the selected Endemic districts of Tanzania'* is my original research conceived for the PhD programme and the results of this work have not yet been previously published.

I, Upendo John Mwingira have made substantial contributions to the conception /design of the work; or the acquisition, analysis or interpretation of data for the work; AND

I have drafted the work or revised critically for important intellectual content; AND

I agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Acknowledgement

I would like to acknowledge the great help given to me by my supervisors Prof. Michael Hoelscher Dr. Inge Kroidl of LMU and Dr. Mwelecele Malecela, former Director General of the National Institute for Medical Research (NIMR) and currently working with WHO-AFRO for guidance in producing this work. Thank you for your sustained encouragement and tireless guidance throughout this study.

I recognize the contributions and help accorded by my colleagues Mr. Mathias Kamugisha from the National Institute for Medical Research (NIMR) in data analysis of this study and Prof Edwin Michael for ideas on sample size calculations.

I am also grateful to Center Neglected Diseases (CNTD- Liverpool) for financing part of data collection. I am greatly indebted to my colleagues at NIMR & NTD programme for their support in data collection. Special acknowledgement to study participants for giving their precious time in this study as well as the required samples.

I also wish to thank Ministry of Health and NIMR Tanzania authorities for granting permission to study and travel abroad during my studies. Sincere gratitude to the former and current Directors of Preventive Services, Donan W Mmbando and Dr. Neema Rusibamayila respectively for their encouragement and for closely following up my progress.

I wish to express my sincere gratitude to my ever loving husband Edmund, daughters Gladys and Gloriousmary and one and only son Edmond for your unwavering love and for always allowing me to be far from home. Surely, you sacrificed a lot during this time. To my mother in-law, siblings and in laws, I am and have been always counting on you all. The reward for this work is ours!!

I dedicate this PhD to my late mother Mary John Mwingira. I drafted the concept paper for this PHD while I was on maternity leave. At this time she was on her last days fighting cervical cancer in my house. She supported in ideas and language despite the fact that she was a non-health related personnel. My parents (Mary and John Cassin Mwingira) have been a great motivation to me and have greatly contributed to all my achievements to date. I thank them for their moral support and enthusiasm on achieving more education than they had. My late mother and auntie were gender activists and have done a lot in the area of "education for a girl child". *I will never let you down and –I always love you -Rest in Peace!!!*

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Affidavit

Upendo John Mwingira

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Zip code, town

Country

I hereby declare that the submitted thesis entitled

“Evaluation of the health impact of Integrated helminth control by Preventive chemotherapy in the selected endemic districts of Tanzania”,

is the result of my own work. I have only used the sources indicated and have not made unauthorised use of services of a third party. Where the work of others has been quoted or reproduced, the source is always given.

The submitted thesis or parts thereof have not been presented as part of an examination degree to any other university.

I further declare that the electronic version of the submitted thesis is congruent with the printed version both in content and format.

Dar es Salaam,28th April 2017 Upendo Mwingira

Evaluation of the health impact of Integrated helminth control by Preventive chemotherapy in the selected endemic districts of Tanzania