KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY

COLLEGE OF HEALTH SCIENCES

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DEPARTMENT OF CLINICAL MICROBIOLOGY

IMPACT OF MASS DRUG ADMINISTRATION OF IVERMECTIN AND ALBENDAZOLE ON THE PREVALENCE OF LYMPHATIC FILARIASIS IN THE NZEMA EAST AND AHANTA WEST DISTRICTS

BY

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By

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DECLARATION

I hereby declare that this submission is my own work towards the MPhil Degree and that, to the best of my knowledge, it contains no material previously published by another person nor material which has been accepted for the award of any other degree of the University except where due acknowledgement has been made in the text.

N. K. O. Ayisi-Boateng …….....

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PG4965010 Signature Date

Certified by:

Prof. K. Ohene-Adjei .....

.....

(SUPERVISOR) Signature Date

Certified by:

Prof. E.H. Frimpong .....

.....

(HEAD OF DEPARTMENT) Signature Date

DEDICATION

To the beautiful ladies in my life from whom I draw inspiration and strength to live my dream and aspire to greater heights;

My wife, Esinam

And

My daughters, Abena Oforibea and Yaa Asieduaa

ABSTRACT

Lymphatic filariasis (LF) is considered a public health problem by WHO. The Global Programme to Eliminate Lymphatic Filariasis (GPELF) targets <1% prevalence by 2020. After more than a decade of implementing the annual mass administration of ivermectin and albendazole in Ghana, this study was conducted to assess its impact on LF prevalence in the Ahanta West and Nzema East Districts of the Western Region. A total of 2,626 adults living in the endemic communities were recruited and tested for microfilaraemia (mf) and circulating filarial antigen (CFA). The study participants were also interviewed to determine the number of rounds of ivermectin and albendazole received. The survey revealed 15.6% of the study participants tested positive for mf whilst 39.2% were positive for antigenaemia. Prevalence rates of mf and antigenaemia among the males were 20.9% and 44.4% respectively, higher than in females who recorded mf and antigenaemia prevalence of 5.8% and 29.7% respectively. The prevalence of lymphedema was 10.1% and that of hydrocele was 40.3%. The prevalence rates were generally higher in younger age groups between 18 and 40 years but declined as the ages increased. The prevalence rates of mf, antigenaemia, hydrocele and lymphedema decreased as the number of MDA rounds increased. After more than ten years of the MDA programme, 97% of study participants had received less than 6 rounds of ivermectin. Non-compliance was higher in males than females and the age group with the highest level of non-compliance was 18-30 years. Prevalence rates among participants who had received at least 7 rounds of ivermectin were <1%. The MDA programme is therefore an effective way of reducing the prevalence of LF and its pathologies. High non-compliance by people living in endemic areas contributes to the

persistently high prevalence rates. This poses a threat to the target to eliminate lymphatic filariasis by 2020 and hence a strategy must be employed to ensure a sustained success.

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LIST OF ABBREVIATIONS

ADLA – Acute Dermato-lymphangio-adenitis

CDC – Centre for Disease Control

CFA – Circulating Filarial Antigen

DEC – Diethylcarbamazine

GFEP – Ghana Filariasis Elimination Programme

GPELF - Global Programme to Eliminate Lymphatic Filariasis

IVM – Ivermectin

LF – Lymphatic Filariasis

MF - Microfilariae

MDA – Mass Drug Administration

NTD – Neglected Tropical Disease

WHO – World Health Organization

VEGF – Vascular Endothelial Growth Factor

ACKNOWLEDGEMENTS

"If I have seen further it is by standing on the shoulders of giants"-Sir Isaac Newton

I am grateful to my Heavenly Father for granting me wisdom, life and good health which enabled me to complete this work and then my earthly father, Mr. George Ayisi-Boateng, who has always believed in me and offered me great opportunities that have brought me this far.

I appreciate the guidance and tutelage of Prof. Ohene Adjei and Dr Alex Debrah, who both worked as my supervisors. Prof. E. H. Frimpong, the Head of Department, and all the lecturers at the Department of Clinical Microbiology, School of Medical Sciences, also gave very useful suggestions which were used to make this work complete.

My appreciation also goes to the team at the Kumasi Centre for Collaborative Research into Tropical Medicine (KCCR) whom I worked with on the field and in the laboratory. Those who deserve special mention are Jubin Osei-Mensah and Daniel Antwi-Berko who provided me with tremendous support. I am also grateful to Linda, Henry, Yussif, Wiredu and Philip.

Special thanks go to the District and Regional Health Directorates of the Ahanta West and Nzema East Districts of the Western Region and to the Chiefs and people living in the study area.

Finally, I wish to express my profound gratitude to my life partner and bedmate, Dr Mrs. Esinam Ayisi-Boateng for the love and understanding she showed in order that I would

have the peace of mind to complete this work. And to my daughters, Abena Oforibea and Yaa Asieduaa, I say, “I love you and thanks for being there”.

CHAPTER 1- INTRODUCTION

Background and Rationale

Lymphatic filariasis is a parasitic infection caused by filarial nematodes. It is classified among a group of infectious diseases called Neglected Tropical Diseases (NTDs). Poverty and low socioeconomic conditions contribute significantly to the incidence of these diseases. The main countries that have the lowest human development indices (HDI) are also reported to have the highest incidence of Neglected Tropical Diseases (Lindoso *et al*., 2009). Currently, an estimated 120 million people are infected in 83 countries throughout the tropics and sub-tropics of Asia, Africa, the Western Pacific, and parts of the Caribbean and South America. About 512 million people are at risk of infection in sub-Saharan Africa and 43 million people are reported to be suffering from complications of the disease. Out of this, at least 25 million men suffer from uro-genital manifestations of varying degrees (Dreyer et al., 2002). This is predominant in developing countries with Africa alone accounting for approximately 40% of the global burden of the disease (WHO, 1994).

In Ghana, there is a high prevalence of microfilaraemia and clinical disease of lymphatic filariasis in the northern guinea savannah and the southern coastal savannah. The middle forest belt is considered relatively free (Gyapong *et al.,* 1996).

It is now known that, contrary to an earlier belief based on blood smears, filarial infection is common in childhood. As many as one-third of children under five years may already have acquired adult worms in endemic areas (Witt, 2001).

The World Health Organization ranks lymphatic filariasis as the second leading cause of disability in the world (Dreyer et al., 1997; Richens et al., 2004). It causes disability such as lymphedema (oedema of the leg) and hydrocele (fluid accumulation in the scrotum) in affected patients.

Patients in developing countries suffering from uro-genital disorders and other pathologies from lymphatic filariasis are faced with a gamut of socio-economic challenges such as stigmatization, sexual dysfunction, loss of spouses and unemployment with the attendant effect on their dependants. (WHO, 2002).

Wuchereria bancrofti, Brugia malayi and Brugia timori are the three major causative organisms for lymphatic filariasis with the mosquito as the vector. About 90% of infected people have bancroftian filariasis and less than 10% have brugian filariasis. In Ghana, lymphatic filariasis is caused by *Wuchereria bancrofti* and Anopheles mosquito is the vector (WHO, 2002).

The life cycle of the *Wuchereria bancrofti* involves developmental phases through the mosquito vector and the human host. During a blood meal, an infected mosquito releases the third stage

filarial larvae (L3) into the human blood. The larvae migrate to lymphatic vessels, develop into adults who mate and produce millions of microfilariae. The microfilariae circulate in the peripheral blood till another mosquito bite. Then the cycle begins. In adult men the preferred site for the adult worms appears to be the intrascrotal lymphatic vessels (DeVries, 2002). The adult worms live in 'nests' within the lymphatic vessels where they cause lymphatic dysfunction through dilatation of the vessels (Dreyer *et al.*,2000).

In response to a resolution by the World Health Assembly in the year 1997, the World Health Organization launched the Global Programme to Eliminate Lymphatic Filariasis (GPELF) whose principal objective is to eliminate lymphatic filariasis globally by 2020.

The Global Programme to Eliminate Lymphatic Filariasis (GPELF) has two major goals: to interrupt transmission of the parasite and to reduce morbidity associated with chronic filarial disease. In 1998, the GPELF recommended annual mass treatment for community members living in endemic areas with two-drug regimens; albendazole plus either ivermectin or Diethylcarbamazine.

A single dose of 400 mg of albendazole decreases *W. bancrofti* microfilaraemia for 6–12 months, and when it is used in combination with ivermectin (or diethylcarbamazine), the numbers of microfilariae in lymphatic filariasis are reduced for longer times than after a single dose of ivermectin. Albendazole is also known to have secondary benefits against intestinal helminths (Dickson *et al.,* 2007; Ottesen *et al*., 1997).

Ivermectin lowers the microfilarial load in affected individuals and temporarily sterilizes adult female filarial worms, thereby reducing transmission and mitigating the clinical manifestations of the infection (Awadzi *et al*., 1999). Although ivermectin is able to kill most of the microfilariae, it has little or no effect on the infective macrofilariae or the adult worm (Hoerauf, 2008; Debrah *et al.,* 2006).

A single dose of 150-200 µg/kg of ivermectin yields maximal microfilarial clearance and hence this is the recommended dosage for lymphatic filariasis control programmes (Debrah *et al.*, 2006). Some microfilaraemic individuals experience adverse events after treatment with ivermectin. This can be attributed to host inflammatory responses to dying microfilariae and not because of drug toxicity (Brown et al. 2001). The fear of experiencing these adverse events sometimes contribute to non-compliance to the treatment for lymphatic filariasis. The addition of albendazole does not appear to increase the frequency or intensity of events seen with ivermectin when used alone (Horton *et al.,* 2000).

A single dose of ivermectin can reduce filarial infectivity by > 80% after six rounds of treatment as revealed in a study in India (Ramaiah *et al.,* 2002). It was also shown that administering both ivermectin and diethylcarbamazine (DEC) reduced the human infection rates by 85-90% after four rounds of treatment with a concomitant reduction in circulating filarial antigen (CFA).

There was also a reversal in pathologies such as hydrocele and lymphedema (Ramaiah *et al.,* 2002).

In another study in Ghana from 1996 to 1998 to assess the effect of ivermectin and albendazole treatment combination, the results showed that ivermectin alone and the combination therapies reduced microfilaria intensities significantly as compared to the placebo group (Dunyo *et al*., 2000).

In order to fully interrupt infection transmission, reduce microfilaraemia and prevent progression of disease, the WHO recommends that the annual mass drug administration (MDA) should be implemented in an endemic community continuously for 4-6 years, which is the average life span of an adult filarial worm. People living in such communities should also comply with and continuously participate in the programme and achieve a minimum coverage of 65% (WHO).

One factor that poses a threat to the success of the MDA is non-compliance among people in endemic communities. In Orissa, India, research showed that 67% of people older than 2 years had received the drugs during MDA and 42% had consumed them. About 25% of people had not taken the tablets although they received them. Urban areas recorded lower rates of non-compliance than rural areas (Babu *et al.,* 2004).

In general, the term compliance describes the extent to which a person's behavior coincides with medical advice (Urquhart, 1994) and compliance with health services is also determined by awareness, acceptability, availability, accessibility and affordability. In another study conducted in India in 2012, 300 households were sampled for MDA compliance. Low acceptability of drug administrator, low acceptability of drug and unfavorable provider attitude were factors determining noncompliance (Nujum *et al.,* 2012).

In spite of the devastating impact of lymphatic filariasis on third world countries it has received little attention in the area of research and active public health activity to bring it under control. Since the inception of the MDA, not much work has been done in Ghana to assess its impact and how it has reduced the prevalence of the infection. There is therefore scanty literature available.

Gyapong *et al*. (1996) conducted a study in the Ahanta West District of the Western Region of Ghana and concluded that it was possible to obtain reliable and valid estimates of the burden of lymphatic filariasis at community level using cheap and non-invasive methods such as key person interviews, focus group discussions, self-administered questionnaires and physical examination of patients. In that study, an examination of a random 30-40 adult males provided a prevalence for hydroceles which gave a good correlation with the community microfilaria prevalence.

Aim

The main objective of this study was to assess the impact of the mass drug administration (MDA) of ivermectin (IVM) and albendazole on the prevalence of lymphatic filariasis.

Specific Objectives

The specific objectives were;

1) To assess the effect of number of rounds of ivermectin (IVM) and albendazole on infection (microfilaraemia and antigenaemia) in Nzema East and Ahanta West districts.

2) To assess the effect of the ivermectin and albendazole rounds on the prevalence of lymphedema and hydrocele pathologies in Nzema East and Ahanta West districts.

3) To assess the effect of persistent non-compliance to ivermectin and albendazole treatment on prevalence of lymphatic filariasis.

CHAPTER 2- LITERATURE REVIEW

Lymphatic filariasis – Parasite, Host and Vector Dynamics

Lymphatic filariasis is a parasitic infectious disease caused by three species of thread-like nematodes, *Wuchereria bancrofti, Brugia malayi and Brugia timori.* It comes only second to malaria as the most disabling mosquito-borne disease (Manguin *et al* 2010). *Wuchereria bancrofti* accounts for approximately 90% of all infections followed by *Brugia malayi* then *Brugia timori* which are prevalent in Asia. They belong to the family *filarioidea* (WHO, 2013).

W. bancrofti derived its name from a physician, Otto Wucherer and a parasitologist, Joseph Bancroft. Both scientists conducted extensive studies into filarial infections. *W. bancrofti* exhibits considerable sexual dimorphism. The adult worm is long, slender, and smooth with rounded ends. It has a short cephalic region and dispersed nuclei throughout its body cavity, with no nuclei at the tail tip. The male worm measures about 3-4cm while the female worm measures 8-10cm.They live for 6-8 years during which period they produce millions of microfilariae, the infective larvae. The male and female worms have a predilection for the lymphatic system which is part of the immune system.

In humans the adult worms mostly lodge in the lower part of the body in the afferent lymphatic channels where they cause lymphangiectasia, disruption of the immune system and fluid accumulation in tissues, particularly in the legs and scrotum (WHO, 2002). In the legs they cause lymphedema, commonly called elephantiasis and in the scrotum they cause hydrocele. These can be a source of severe pain and profound disability to the affected patients (WHO, 2002).

The mosquito is the vector involved in the transmission of the infective larvae. There are at least 43 species of the *Anopheles* mosquito that transmit the infection in West Africa, rural Southeast Asia and parts of the Southern Pacific; 6 species of the *Culex* mosquito infect humans in East Africa, Middle East, urban Southeast Asia and Latin America whilst the *Aedes* mosquito, which has 20 different species among them, is common particularly in the Pacific islands and parts of Southeast Asia (Manguin *et al.*, 2010).

All mosquito species require water to breed hence they are common in water-stagnating environments such as choked gutters, pools and ponds, flooded areas and water collected among weeds. Most species of mosquitoes especially the *Anopheles* are crepuscular (active at dusk or dawn) or nocturnal (CDC, 2013). Mosquitoes may be anthropophilic (bite humans) or zoophilic (animal-biting). The male mosquitoes live for about a week and feed on nectar and other sources of sugar. The female mosquitoes can survive for up to a month and also feed on sugar as a source of energy. They however depend mainly on blood meal since they require blood for the production of eggs. Their chances of survival depend on temperature and humidity, success at obtaining a blood meal and ability to avoid host defenses. Some Anopheles mosquitoes prefer to rest and feed outdoors (exophagic) whilst others rest and feed indoors (endophagic). They are attracted by exhaled carbon dioxide and human odour (CDC, 2013).

Life Cycle of Wuchereria bancrofti

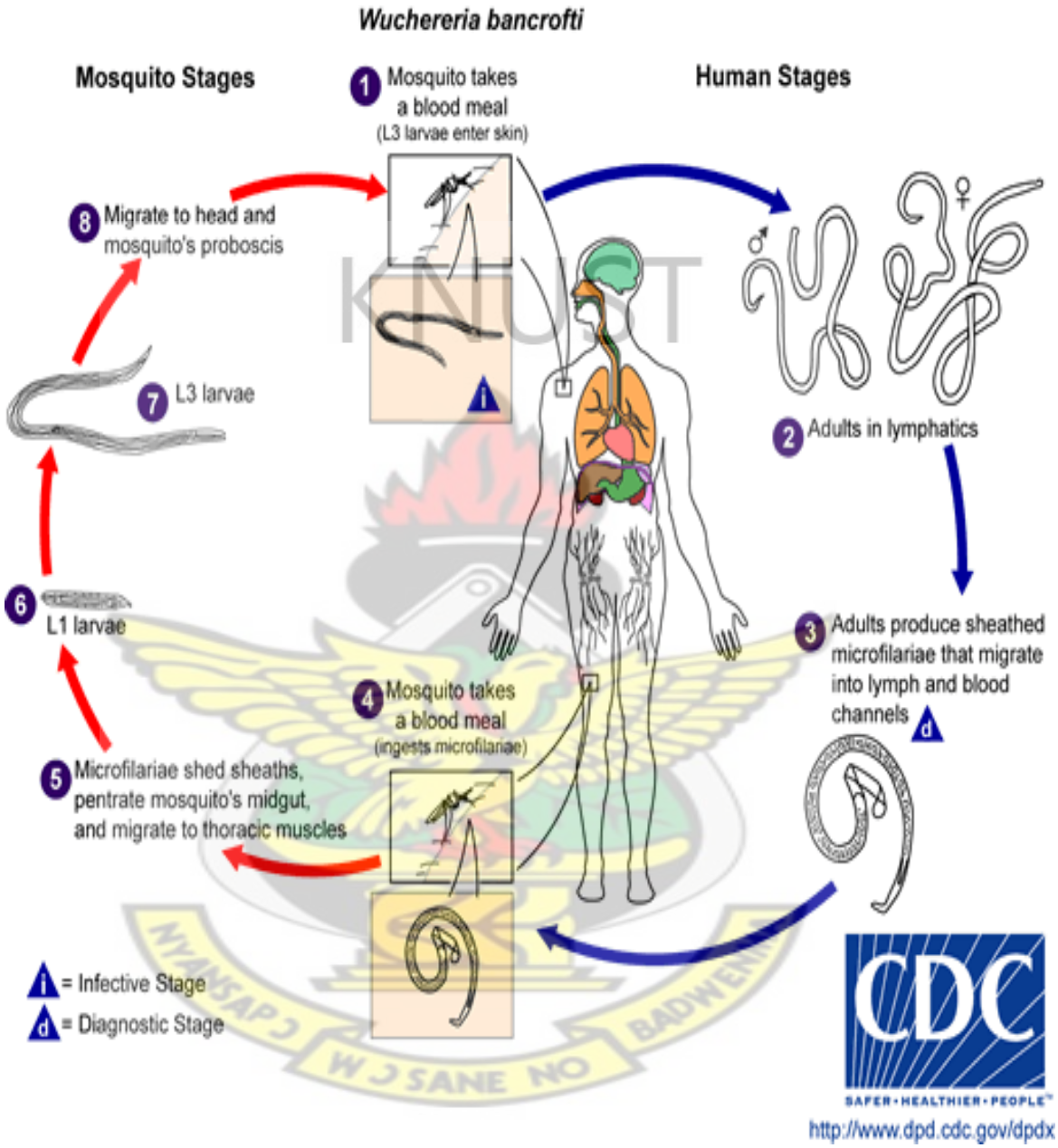


Figure 1.1: Life Cycle of *Wuchereria bancrofti*

In the life cycle of the parasite, it has two hosts. The mosquito vector is the intermediate host and human beings are its definitive host. There is no reservoir host. During a blood

meal, an infected mosquito introduces third-stage filarial larvae onto the skin of the human host, where they penetrate into the bite wound. They develop into adult worms that commonly reside in the lymphatics. The adult worms produce microfilariae which are sheathed and have nocturnal periodicity, except the South Pacific microfilariae which do not exhibit periodicity. The microfilariae move actively through lymph and blood and find their way into lymph and blood vessels. A mosquito ingests the microfilariae during a blood meal. After ingestion, the microfilariae lose their sheaths and some migrate through the mosquito's midgut to reach the thoracic muscles. There the microfilariae develop into first-stage larvae and subsequently into third-stage infective larvae. The third-stage infective larvae migrate through the hemocel to the mosquito's proboscis and can infect another human when the mosquito takes a blood meal. The mosquito remains infectious for only 10-14 days after consuming an infected blood meal (Manguin *et al*. 2010)

Clinical Manifestations of Lymphatic filariasis/Pathogenicity

People living in endemic areas for lymphatic filariasis can be classified into three main groups (Melrose, 2002);

i. Endemic normals who have been exposed to the nematode but have not been infected

ii. Those who have been exposed, infected and have microfilaria in their blood, but remain asymptomatic

iii. Those who are chronically infected and present with lymphedema and hydrocele.

The third group can also present with Acute dermato-lymphangio-adenitis (ADLA) which usually occurs when an adult worm dies and the lymph vessels surrounding it are inflamed due to the host's immunological response (Melrose, 2002; Pfarr *et al.,* 2009). It is common in older children and youth and remains with the infected individual throughout life. It commonly manifests as fever, chills, swelling and lymphedema. Chronic ADLA attacks can result in renal disease, haematuria, proteinuria, chyluria, nephritic syndrome and glomerulonephritis (Pfarr *et al*., 2009; Melrose, 2002)

Patients with lymphatic filariasis can also suffer from rheumatic disorders, cystitis with urethral obstruction, fibrosing mediastinitis, tropical vaginal hydroceles and bladder pseudotumors. Pulmonary eosinophilia, characterized by paroxysmal cough and wheezing is another feature of lymphatic filariasis. Such patients may test negative for microfilaraemia but may harbour the adult worms (Melrose, 2002).

The most disabling of the pathologies associated with lymphatic filariasis is elephantiasis, a permanent swelling of a limb, usually the lower limbs. The condition worsens when there is super-infection by *Streptococci* bacteria (Melrose, 2002; Shenoy, 2008).

Factors that may predispose a patient to chronic filarial disease include a dose of the infectious agent, a pre-existing bacterial infection or a specific host response (Dreyer *et al*., 2000). There is also evidence that there is a genetic trait for the development of an extreme form of pathology and that genetic polymorphism in vascular endothelial growth factors are associated with disease states (Debrah *et al*., 2007).

Hydrocele

The World Health Organization estimates that about 25 million men suffer varying degrees of urogenital manifestations of lymphatic filariasis. These include penoscrotal lymphedema and hydrocele (Dreyer *et al*., 2002). Hydrocele is simply defined as the accumulation of fluid in the tunica vaginalis and can be a source of psychological, social, marital and economic distress to the patient (WHO, 2002). In spite of its debilitating impact on the male population, filarial hydrocele is the pathology that has received the least attention by the Global Programme to Eliminate Lymphatic Filariasis (GPELF) (Addis *et al*., 2007).

W. bancrofti is the only lymphatic filarial parasite that induces genital diseases. The pathogenesis of penogenital lymphedema and filarial hyrdocele is poorly understood but can be partly explained by the fact that the adult worms appear to prefer residing in lymphatic vessels in the lower part of the human body. In adult men the preferred site for the adult worms appears to be the intrascrotal lymphatic vessels (DeVries, 2002).

A pilot study undertaken by Debrah *et al* (2007) demonstrated a genetic basis for hydrocele pathology. People who are prone to producing VEGF-A are susceptible to the pathology. Vascular endothelial growth factors (VEGFs) are required for vasculogenesis and also for physiologic and pathologic angiogenesis.

Figure 1.2 Hydrocele

VEGF-A is a major mediator of vascular permeability and angiogenesis and promotes extravasation of fluid and plasma proteins from the blood vessels. *Wolbachia* in *Wuchereria bancrofti* elicits the over-expression of lymphangiogenic and vascular factors such as VEGF-A (Awata *et al.,* 2002; Ray *et al*., 2004).

A case-control study of VEGF-A single nucleotide polymorphisms (SNPs) demonstrated that hydrocele is associated with a SNP in the VEGF-A promoter that leads to the production of more VEGF-A and can predispose people to this disease phenotype (Debrah et al., 2007). A follow up study conducted in 2009 also showed that targeting the *Wolbachia* endosymbionts by doxycycline, an antibiotic, led to a reduction of *Wolbachia* numbers and death of the adult filarial worm. These resulted in amelioration of the size of the hydrocele through reduction of plasma levels of VEGF-A (Debrah et al. 2009).

Lymphedema

Lymphatic filariasis is the commonest cause of lymphedema in endemic countries. It is estimated that among 120 million infected people in 83 countries, up to 16 million suffer from filarial lymphedema (Bundy *et al*., 1996). It is a chronic condition which evolves slowly over a long period of time. Commonly it affects the lower limbs but it may also involve the arms, the male and female genitalia and very rarely breasts (Pani *et al*., 1995).

Affected patients very often go through significant psychological trauma, social stigmatization, sexual dysfunction and economic challenges resulting in loss of confidence and sometimes depression (Pani *et al.,* 1995; Ramaiah *et al.,* 1998; 2000).

These result not only from the deformities caused by lymphatic filariasis but also from the recurrent acute febrile episodes associated with the disease (Pani *et al.,* 1995; Ramaiah *et al.,* 1998; 2000).

Dilation of lymph vessels is the earliest structural change in lymphatic filariasis. This is where the adult worms are found and can be demonstrated in subjects who are clinically asymptomatic except for presence of microfilariae (mf) in blood, by ultrasound examination of lymphatics of the spermatic cord; lymphoscintigraphy of the limbs and by direct examination of lymph vessels resected by surgery (Freedman *et al*., 1994; Noroes *et al*., 1996).

As the dilation and damage to the lymphatic vessels progress, there is stasis of lymph in the lymphatic vessels as a result of incompetence of the valves within the vessels. Lymph stagnation serves as a medium for bacterial growth and the damage of lymphatic vessels is worsened by bacterial infections of the limb, prolonged standing or by strenuous exertion (Shenoy, 2008).

In advanced stages of lymphedema the skin is thickened and thrown into folds, often with hypertrichosis, black pigmentation, nodules, warty growth, intertrigo in the webs of toes or chronic non-healing ulcers. There are commonly fungal infections in-between the toes and skin folds (Burri *et al.,* 1996).

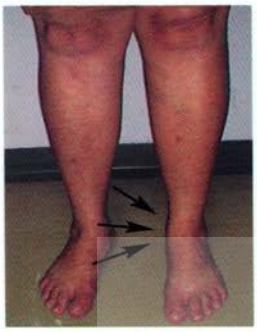
In early stages of lymphedema, antifilarial drugs such as diethylcarbamazine (DEC) are used for treatment. To prevent acute attacks characterized by fever and chills, antibiotics and antifungals may be employed (Shenoy, 2008). Other non-pharmacological measures that have been practiced are limb-hygiene, use of elasto-crepe bandage, elevation of

affected limb at night, regular exercise of affected limb and massage of limb especially in early oedema (Shenoy, 2008). Surgical procedures that are sometimes performed to provide relief in severe cases of lymphedema are lymph nodo-venous shunts, omentoplasty and excision plus skin grafting (Pani *et al*., 1998).

It is more imperative that efforts are made to prevent lymphedema from developing than to treat it. This is because studies have shown that once the lymphatic damage is established it cannot be reversed even with treatment (Freedman *et al.*, 1995). Primary prevention is possible through the Mass Drug Administration programme instituted by the Global Programme to Eliminate Lymphatic Filariasis (GPELF). Secondary prevention is aimed at treating the early infection with antifilarials to prevent the progression to lymphedema (Shenoy, 2008).

Clinical staging of lymphedema is as follows (Dreyer *et al*);

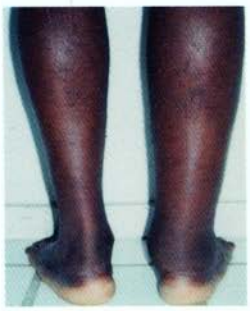
LYMPHOEDEMA STAGING AND MANAGEMENT FOR FILARIASIS–ENDEMIC AREAS



Stage 1

Characteristic feature: Swelling is reversible (goes away) overnight.

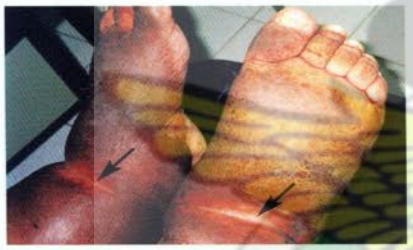
In stage 1 lymphoedema, the swelling increases during the day and goes away overnight when the patient lies flat in bed. To accurately classify lymphoedema in patients with stage 1 disease, it is best to examine the leg in the late afternoon, when the swelling is most visible, and again in early morning, to see that the swelling is gone. If there is swelling in both legs, it may be necessary to rely on the patient's report of normal-size legs in the morning, because comparison with the patient's "normal" leg is not possible.



Stage 2

Characteristic feature: Swelling is not reversible (doesn't go away) overnight.

The main difference between stage 2 lymphoedema and stage 1 is that the swelling does not go away without lymphoedema management. Occasionally, patients with stage 2 lymphoedema will have acute attacks. They also may have entry lesions between the toes, and a mild bad odor.



Stage 3

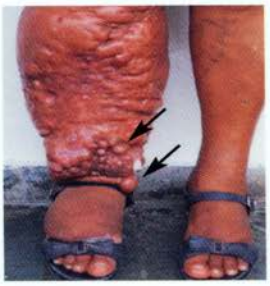
Characteristic feature: Shallow skin folds.

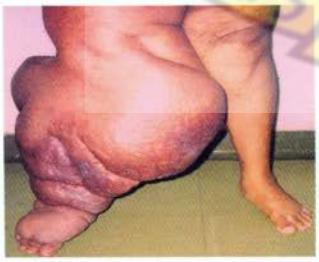
The principal feature of stage 3 lymphoedema is the presence of one or more shallow skin folds. Shallow folds are those in which the base of the fold can be seen when the patient moves the leg or foot so that the fold "opens up". Even very thin lines or creases, which are not seen on normal legs, are considered shallow folds. Early shallow folds are much easier to see when the patient is standing. Thus, it is important to have the patient standing when you are staging the lymphoedema.

Stage 4

Characteristic feature: Knobs.

The main feature of stage 4 lymphoedema is the presence of knobs. Knobs are bumps, lumps, or protrusions of the skin. The importance of knobs comes from the fact that they predispose the leg to further trauma and, therefore, to additional entry lesions, especially if the skin at the site of the knob is less sensitive than the surrounding skin.





Stage 5

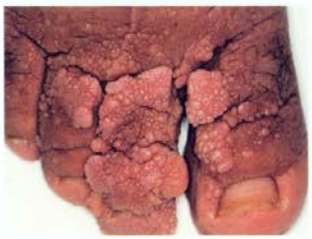
Characteristic feature: Deep skin folds.

The presence of one or more deep skin folds is the main feature of stage 5 lymphoedema. Deep folds are those whose base cannot be seen when the patient moves the leg or foot so that the fold "opens up"; rather, the base of the fold can be seen only when the edges are actively separated by hand.

Plate 2.1 Lymphedema Staging (1-5) and Management (Source; Dreyer *et al*., 2002)

Stage 6

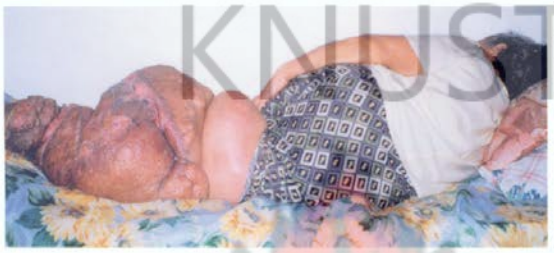
Characteristic feature: Mossy lesions.



On the surface of the skin (especially the upper surface of the toes), very small elongated or rounded small growths may develop. They are usually clustered together, giving rise to the peculiar appearance of "mossy lesions". When located on the foot, this condition is known as "mossy foot". Rarely, these lesions can appear on the leg.

Stage 7

Characteristic feature: Unable to care for self or perform daily activities.



The patient is unable to adequately or independently perform routine daily activities such as walking, bathing, or cooking, etc. Patients with stage 7 lymphoedema have frequent acute attacks and large legs, usually with deep folds. They always have entry lesions between the toes and skin folds. The bad odor is very strong. Wounds in the skin are commonly present, and lymphoedema extends above the knee in most patients. The principal feature of stage 7 lymphoedema is that the patient cannot perform daily activities. Assistance from the family and the health care system is needed.

LYMPHOEDEMA MANAGEMENT, BY STAGE

Treatment Component	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Stage 6	Stage 7
Hygiene (washing and drying)	Yes (ideally at night)	Yes (ideally at night)	Yes (ideally at night)	Yes (ideally at night)	Yes (twice a day if possible)	Yes (twice a day if possible)	Yes (twice a day if possible)
Care of entry lesions	If present	If present	If present	If present	If present	If present	If present
Exercise	Yes	Yes	Yes	Yes	If possible	If possible	If possible
Elevation	Usually not necessary	At night	Day and night	Day and night	Day and night	Day and night if possible	Day and night if possible
Prophylactic creams	No	No	Usually not necessary	Usually not necessary	Usually necessary	Necessary	Necessary
Prophylatic systemic antibiotics (send to doctor)	No	No	No	Usually not necessary	Usually necessary (if acute attacks persist)	Necessary	Necessary
Cosmetic surgery	Not applicable	Not applicable	Not applicable	If medically indicated	If medically indicated	If medically indicated	If medically indicated

Plate 2.2 Lymphedema Staging (6-7) and Management (Source; Dreyer *et al.*, 2002)

Figure 1.3 Elephantiasis (Source; Original)

Acute Dermato-lymphangio-Adenitis (ADLA)

This is the commonest acute clinical manifestation of lymphatic filariasis and it usually results from the inflammation of lymphatic vessels due to the death of adult worms (Melrose, 2002; Pfarr *et al.*, 2009). The patient usually complains of fever, chills, pains in the affected limb and vomiting. On examination there is often erythema of the skin, enlarged inguinal and axillary lymph nodes and local tenderness. In very severe cases in which there is toxaemia, there may be altered sensorium and, sometimes, urinary incontinence (Shenoy, 2008).

Currently studies have shown that the filarial worms are not directly responsible for the onset of ADLA (Dreyer et al 1999) but that these acute attacks are as a result of bacterial infections (Shenoy *et al*., 1995;1998;1999).

In India, surveys conducted in Pondicherry and Sherthallai estimated the frequency of ADLA in Bancroftian filariasis as 4.47 episodes per year and 2.2 episodes per year for brugian filariasis (Panicker *et al.,* 1990). The duration of such attacks averages about 4 days but this depends largely on its severity. Some precipitating factors that affect ADLA may be paronychia, eczema or severe fungal infections in the webs of toes.

The mode of treatment instituted depends on the severity of the ADLA. In mild cases, simple analgesia and elevation of affected limbs may be indicated. In moderate to severe cases, oral antibiotics and anti-fungals, and in some cases, parenteral antibiotics are administered. Commonly used antibiotics are penicillin, amoxicillin, doxycycline and cotrimoxazole (Shenoy, 2008).

Common drugs employed in the Treatment and Control of Lymphatic Filariasis

Diethylcarbamazine (DEC)

Diethylcarbamazine was discovered in 1948 and has been established as the drug of choice for the treatment of filariasis. From the late 1940s until the 1990s it remained the only useful drug for community filariasis control (Taylor *et al.,* 2010; Awadzi *et al.,* 1992).

It is helpful in early stages of lymphatic filariasis because once the lymphatic damage is established, administering DEC does not reverse the pathology (Freedman *et al.,* 1995; Addiss *et al.,* 2000).

The mode of action of diethylcarbamazine is still not completely understood, but it results in the sequestration of mf and their eventual destruction by the immune system. Studies have shown that DEC kills microfilariae, but repeated doses are needed before adult worms are killed or sterilized and that when given in low dose over a period of months or years, DEC is effective in reducing the prevalence of filariasis in communities, with no recognized adverse effects (Adinarayanam *et al.,* 2009).

For a long time, it has been widely accepted that the recommended dose for DEC should be 6mg/kg daily for 12days but studies conducted by Gyapong *et al* (2005) have suggested that a single dose of 6mg/kg is as effective as that given over a 12-day period. Both regimen are able to kill the microfilariae and adult worms.

Ivermectin

Ivermectin (22,23-dihydroavermectin B_{1a} + 22,23-dihydroavermectin B_{1b}) is a broad-spectrum antiparasitic agent which acts by hyperpolarization of glutamate-sensitve channels and was recently shown to block the contractile activity of the excretory/secretory vesicles. It is effectively microfilaricidal and has also been shown to partially interrupt embryogenesis after frequent administration (Pfarr *et al*., 2006; Awadzi *et al.*, 1999).

Ivermectin is contraindicated in children under-five years and those weighing less than 15kg (Dourmishev *et al.*, 2005). Also, it should not be given to those with hepatic or renal disease, pregnant women and those breastfeeding children younger than one week old (Tielsch *et al.*, 2004).

The standard dose for ivermectin is 150-200 µg/kg. A single dose as high as 1600 µg/kg does not affect its effectiveness but may, at best, lead to a mild-to-moderate macrofilaricidal affect after repeated standard doses (Awadzi *et al.*, 1999).

Adverse effects associated with ivermectin usually corresponds with the microfilarial load and these include fever, rigors, pruritic rash, oedema of the face and limbs, weakness and myalgia (Taylor *et al.*, 2010).

A study conducted in India with 34,000 people revealed that the strategy to annually administer a single dose ivermectin was as effective as the single dose DEC treatment. Both ivermectin and DEC reduce vector infectivity by > 80% after six rounds of treatment. Administering the two drugs together reduced the human infection rates by 85-90% after four rounds of treatment with a concomitant reduction in circulating filarial antigen and a significant reversal in filarial pathologies like hydrocele and lymphedema (Ramaiah *et al.*, 2002).

In Ghana, a randomized double-blind placebo-controlled field trial was conducted from 1996 to 1998 to assess the effect of ivermectin and albendazole treatment combination for *Wuchereria bancrofti*. Night blood samples were taken after 3, 6 and 12 months to determine the level of microfilaraemia. The results showed that ivermectin alone and the

combination therapies reduced microfilaria intensities significantly as compared to the placebo group (Dunyo *et al.*, 2000).

Albendazole

Albendazole is an antihelminthic belonging to a group of drugs called benzimidazoles and is effective against a wide range of nematodes in both domestic animals and humans. It inhibits the polymerization of worm β-tubulin and microtubule formation. It has also been shown that albendazole inhibits the enzymatic action of fumarate reductase which is helminth-specific.

Albendazole is poorly absorbed from the gastrointestinal tract due to its low aqueous solubility. Albendazole concentrations are negligible or undetectable in plasma as it is rapidly converted to the sulfoxide metabolite prior to reaching the systemic circulation. The systemic antihelminthic activity has been attributed to the primary metabolite, albendazole sulfoxide.

Oral bioavailability appears to be enhanced when it is coadministered with a fatty meal as compared to the fasted state. Albendazole is contraindicated in those who have hypersensitiviy reactions to benzimidazole group of compounds and should not be given to pregnant women because of its teratogenicity.

A single dose of 400 mg decreases *W. bancrofti* microfilaraemia for 6–12 months, and when it is used in combination with ivermectin (or diethylcarbamazine), the numbers of microfilariae in lymphatic filariasis are reduced for longer times than after a single dose of ivermectin. Studies have shown that administering only albendazole did not appear to

reduce mf prevalence when compared with placebo. A combination of albendazole and ivermectin however appeared more effective than either ivermectin alone or albendazole alone (Kshirisagar *et al.*, 2004).

It has also been shown that there is a significant reduction in the prevalence of filarial antigenaemia when albendazole is administered to patients who are co-infected with intestinal helminths but produced little effect in those infected with only Wuchereria bancrofti (Prakash *et al*., 2005).

It was concluded in another study that co-administration of albendazole was more effective in reducing mf prevalence than one antifilarial drug alone (Gyapong et al., 2005).

Global Programme to Eliminate Lymphatic Filariasis (GPELF)

The Global Programme to Eliminate Lymphatic Filariasis (GPELF) was launched in 2000 with the principal objective of breaking the cycles of transmission of *Wuchereria bancrofti* and *Brugia* spp. through the application of annual mass drug administration (MDAs) to entire at-risk populations (Bockarie *et al.*, 2009).

The programme originated from the World Health Assembly Resolution WHA 50.29 which was adopted in 1997 by the World Health Organization. In that year, the WHO classified lymphatic filariasis as potentially eradicable and therefore called on member states to initiate activities and strategies to eliminate the disease as a public health problem. The target is to eliminate lymphatic filariasis by 2020. In response to this call, two pharmaceutical companies GlaxoSmithKline and Merck & Co Inc made a generous

and unprecedented long-term pledge to donate albendazole and ivermectin to support the programme.

The strategy of the GPELF has two key components:

1. Interrupting transmission through annual mass drug administration for the entire at-risk population;
2. Morbidity management and disability prevention to alleviate suffering caused by lymphatic filariasis

Before drugs are administered to any at-risk population mapping is done to identify where to administer annual single doses of albendazole plus either diethylcarbamazine or ivermectin. The WHO recommends that to fully interrupt infection transmission, MDA should be implemented in a community continuously for 4-6 years (WHO).

The major sources of morbidity and suffering in lymphatic filariasis are acute attacks of fever, chills and pains in acute dermatolymphangioadenitis (ADLA), lymphedema and hydrocele. These cause serious disability and incapacitation. Clinical severity of these can be improved by simple measures of hygiene, skin care, exercise and elevation of affected limbs (WHO, 2013). The GPELF aims to provide access to health care for these patients in order to alleviate their suffering and improve their quality of life.

In the WHO 2000-2009 Progress Report on GPELF, it was reported that the programme has been one of the most rapidly expanding global health programmes in the history of public health. During the period 2000-2009, more than 2.8 billion doses of medicine were delivered to a total population of 845 million people. Out of 81 countries where

lymphatic filariasis was considered endemic, 53 of them had implemented the MDA. Five (5) of these countries have achieved the targets for interrupting transmission and have stopped MDA. By the year 2010, 70% (37) of the 53 countries had completed 5 or more rounds of MDA in at least some of their endemic areas and by 2011, 12 countries had moved to the post-surveillance phase.

From 2000 to 2011, more than 3.9 billion treatments were delivered to a targeted population of about 950 million individuals in 53 countries, considerably reducing transmission in many places. Recent research data show that the transmission of lymphatic filariasis in at-risk populations has dropped by 43% since the beginning of the GPELF. The overall economic benefit of the programme during 2000-2007 is conservatively estimated at US$ 24 billion (Ottesen *et al*., 2011).

In a study conducted by Ottesen *et al* (2011) to assess the health benefits of GPELF after 8 years of implementation, the following were revealed;

- Lymphatic filariasis was prevented in an estimated 6.6 million newborns through the participation of women in their reproductive age in the MDA
- Prevention of 4.4 million cases of subclinical disease, 1.4 million cases of hydrocele and 800,000 cases of lymphedema in the lifetime of the estimated 6.6 million newborns
- Out of a total of 9.5 million adults infected with lymphatic filariasis but with no overt manifestations of disease, hydrocele was prevented in 6.0 million of these and lymphedema in 3.5 million.

- 32 million DALYs (Disability Adjusted Life Years) were also averted.
- Since two (albendazole and ivermectin) of the three drugs used in the MDA have broad anti-parasite properties, treated populations are also protected from intestinal worms and skin infections with Onchocerca, lice and scabies

The economic benefits of GPELF have also been enormous. In another study to assess the economic benefits of GPELF after 8 years (2000-2007) of implementation, these were the findings (Chu *et al.*, 2011);

- An estimated US$ 21.8 billion of direct economic benefits would be gained over the lifetime of 31.4 million individuals treated during the first 8 years
- US$ 2.3 billion savings from protecting nearly 3 million newborns and other individuals from LF infection
- Lifetime economic benefits of approximately US$ 19.5 billion as a result of halting disease progression in those already infected with lymphatic filariasis
- Health systems of endemic countries are also saved almost US$ 2.2 billion in decreased patient services as a result of reduced LF morbidity (Chu *et al*., 2011).

GPELF and MDA in Africa

Africa accounts for about 30% of the burden of lymphatic filariasis in the world and 39 African countries are considered endemic with approximately 405.9 million at risk population. The filariasis elimination programme was launched in the year 2000 in Africa and MDA was conducted in four African countries namely, Ghana, Nigeria, Togo and the United Republic of Tanzania. By the year 2009, six African countries, Ghana,

Burkina Faso, Comoros, Malawi, Mali and Togo had achieved full coverage of their entire at-risk population (WHO, 2009). 15 countries in Africa had not initiated MDA and 5 countries were considered unlikely to require MDA. These were Burundi, Cape Verde, Mauritius, Rwanda and Seychelles.

Nine (9) years until the proposed goal of eliminating lymphatic filariasis by 2020, it is mainly African countries in which MDA has not yet begun or is still behind schedule. A combination of ivermectin and albendazole is considered inferior to Diethylcarbamazine and albendazole due to their high macrofilaricidal activities. This may account for the poor expected outcome in regions where multiple rounds of MDA have been performed (Awadzi *et al*., 2004; Osei Atweneboana *et al.*, 2007).

Additionally, areas with LF-Loiasis co-endemicity have not experienced MDA programmes. This is because patients co-infected with *loa loa* when given ivermectin, manifest signs of encephalopathy, correlating with microfilarial load in the spinal fluid (Gardon *et al*., 1997; Carme *et al*., 1991; Wanji *et al*., 2009).

Ghana Filariasis Elimination Programme (GFEP) and MDA

In Ghana, an estimated 11,587,953 people are at risk of infection with lymphatic filariasis (WHO, 2009). Since the year 2000, a National Programme was established to eliminate lymphatic filariasis and onchocerciasis in Ghana through the annual distribution of ivermectin and albendazole to all individuals living in endemic areas.

The Ghana Filariasis Elimination Programme (GFEP), with funding from the Department for International Development (DFID), started a pilot project in 5 districts

from 2001. The districts were Awutu-Effutu Senya, Ahanta-West, Sissala, Kassena-Nankana and Builsa and by the year 2008 the programme had completed 8 rounds of mass drug administration in these 5 districts. There are 82 endemic districts in Ghana all of which have received varying treatments from 3 to 8. Ghana however reached a total national coverage in 2006 and by the year 2008 the GFEP had undertaken 31,053,694 treatments.

The main objective of the GFEP is to reduce the prevalence of lymphatic filariasis to levels that would no longer be of public health significance. The specific objectives are;

1. To break the transmission cycle of lymphatic filariasis through the administration of anti-filarial drugs;
2. To alleviate the suffering of individuals suffering from afflictions due to filarial infections
3. To provide health education on causes, effects and control of lymphatic filariasis disease

The activities employed to achieve the programme goals are;

• Procurement and management of drugs and logistics

• Training for Mass Drug Administration

• Social Mobilisation for Mass Drug Administration

• Mass Drug Administration

• Monitoring and Evaluation

• Advocacy

In 1996, a survey involving all the 10 regions of Ghana was conducted to determine the prevalence and distribution of *Wuchereria bancrofti* microfilaraemia and clinical disease associated with lymphatic filariasis. The results showed a high prevalence of microfilaraemia and disease with the prevalence varying from one region to the other. In general, the disease was more prevalent in the northern guinea savannah and the southern coastal savannah, while the middle forest belt was relatively free (Gyapong *et al*., 1996).

Crowded living conditions, housing quality and inadequate waste disposal and sanitation facilities combined with seasonal migration between endemic rural areas and non-endemic urban areas contribute to the growing urbanization of lymphatic filariasis (Schweinfurth, 1983; MAK, 1986).

CHAPTER 3– MATERIALS AND METHODS

Description of Study Area

The study was conducted in areas endemic for lymphatic filariasis in the Nzema-East and Ahanta-West Districts of the Western Region of Ghana (Dunyo *et al.,* 1996). The Ahanta West District, whose capital is Agona Nkwanta, has a total land area of 591 square kilometres and lies between latitude 4.45ºN and longitude 1.58ºW. The estimated human population in the year 2011 was 126,429 with a projected growth rate of 3.2%. Females make up 51.65% of the population, whilst the males comprise 48.38%. The district is predominantly rural and has about 123 settlements. It is bounded on the east by the Sekondi-Takoradi Metropolis and on the west by the Nzema East District. On the north, it is bounded by Mpohor Wassa East and Wassa Amenfi West Districts and on the south by the Gulf of Guinea. The major economic activity undertaken by the people is farming with about 65% of the active population being involved in agriculture. Some of the people, however, engage themselves in trading, processing of agricultural produce, mainly oil palm, cassava and rubber. Boreholes, streams, hand-dug wells as well as pipe-borne water are some of the sources of water for their household. Fifty-eight percent (58%) of the population has access to pipe-borne water, boreholes and hand-dug wells fitted with pumps (www.mofep.gov.gh).

The Nzema East District is one of the new districts created in the year 2008. Its capital is Axim. It occupies a land area of 2,194 square kilometres and has a population of 60,282 people according to the 2010 Housing and Population Census. The district is located at the southern end of the Western Region between longitudes 2 05º and 2 35º West and Latitudes 4 40º and 5 20º North of the Equator. It is bordered on the west by Ellembelle District, on the north by Wassa Amenfi West District and on the east by the Tarkwa Nsuaem Municipal, Prestea Huni Valley and Ahanta West Districts. On the south is the Gulf of Guinea with about 9km stretch of sandy beaches (www.mofep.gov.gh).

The Nzema East District lies between the Wet Semi-Equatorial Climate zone of the West African Sub-region. Rain falls throughout the year with the highest monthly mean occurring around May and June. The average temperature is about 29.4ºC.

A total of 54 communities were selected for the study. The communities are mainly rural with a number of them located along the coast of the Atlantic Ocean. Sanitation is generally poor in these communities characterized by bushes, weeds, pools of water and choked gutters. These serve as breeding grounds for the mosquito vector. Sources of drinking water are mainly boreholes, hand-dug wells and natural water bodies.

Majority of the indigenes are farmers and fishermen. It is estimated that about 65% of the economic population are involved in Agriculture (i.e. fishing and farming). Most of their houses are made of mud, interspersed with a few block houses.

Study Population

The study population included males and females, 18 years and above, who were living in the endemic communities. Whilst some of the recruited study participants had never participated in the annual mass drug administration of ivermectin and albendazole, the rest had received treatment ranging from 1 to 10 rounds.

Plate 3.1 shows 43 out of the 54 communities selected for this study. The communities in which the study was conducted were Abease, Akyinim, Adukrom, Agyan, Adjua, Akatakyi, Akatenchi, Akonu, Akwidaa Akyinim, Ampatano, Ankyerenyin, Anto Apewosika, Asuboi, Asemasa, Asemkow, Awukyire, Axim Akyinim, Axim Apewosika, Axim Brewere, Bakanta, Breman, Butre Anlo, Busua, Chavani, Cape 3 points, Dumunli, Dixcove, Duahorodo, Dzakpasu, Ehuntumano, Ekyam, Enimakrom, Eyiwaehu Eguafo, Funkoe, Kamfakrom, Kwasikrom, Mpaesem, Medinya, Ndatiem, New Akwidae, New Amanful, Old Akwidae, Princess Town, Pumpunie, Seremowu and Sese Akatayi .

STUDY COMMUNITIES

.Ahanta West District

1.Busua	7.Dixcove	13.Asemasa	19.Asemkow	25. Ampatano
2. Asuboi	8. Akyenim	14.Egyam	20. Ehuntmano	26.Butre
3. Old Akwadaa	9. Cape three point	15.Achowa	21.Kamfakrom	27. New Akwadaa
4. Ketakor	10. Punpunie	16. Seremou	22. Enyiwaehu	28. New Amanful
5. Aketenchie	11.Komanfokrom	17. Aketechi	23. Princes Town	29, Mpeasem
6. Kwasikrom	12.Adjua	18. Duahorodo	24. Funkoe	30.Dzapkasu

•Nzema East District

31.Asanta	33.Sanwoma	35. Ampain	37. Miamia	39. Kikam	41. Esiama	
32.Agyambra	34.Ainyinasi	36. Bakanta	38.Telebokazo	40.Sese	42.Bobrama	43.Azulenuanu

Plate 3.1 Map of the Study Area

Ethical Considerations

Ethical clearance was obtained from the Committee on Human Research Publication and Ethics (CHRPE) of the School of Medical Sciences (SMS), Kwame Nkrumah University of Science and Technology (KNUST). Permission to conduct the study in the selected communities was sought from the Ahanta West and Nzema East District Health Directorates.

The help of community leaders such as chiefs, community health workers and volunteers was also solicited. Participants were informed in detail about the design, the duration and the conditions of the study following the informed consent procedures of Good Clinical Practice

(GCP). Signed or thumb-printed informed consent was subsequently obtained from each study participant.

Study Design

The study was a cross-sectional study that involved recruiting two thousand six hundred and twenty-six (2,626) adult men and women who had been living in the endemic communities. Communities in the Nzema East and Ahanta West Districts were screened with the help of voluntary health workers of the districts. Those willing to participate, after providing written informed consent (sign or thumb print Informed Consent Form (ICF), underwent clinical, and parasitological examinations.

Inclusion Criteria

i. Men and women between 18-65 years old
ii. Willingness to participate in the study as evidenced by signing of the informed consent document (written or thumb print)
iii. Resident in the endemic area

Exclusion Criteria

i. Non-resident in the endemic area
ii. Refusal to sign or thumb-print consent form as evidence of willingness to participate in the study

After recruitment, patients meeting the entry criteria were enrolled into the study. All patients were made to understand that the study was voluntary and were encouraged to ask questions during and after the study.

Study Procedure

Sample Collection

Since the microfilariae of *Wuchereria bancrofti* has nocturnal periodicity, the blood samples of study participants were taken in the evening between 9pm and midnight.

After signing/thumb-printing the informed consent forms, those satisfying the inclusion criteria were first pricked in the index finger to determine the presence of *Wuchereria bancrofti* microfilariae. Ten millilitres (10mls) of venous blood was also taken to quantify the microfilariae and determine the circulating filarial antigenaemia.

Laboratory Examinations

Determination of Circulating Filarial Antigenaemia

TropBio® ELISA test kit (Townsville, Australia) was used to measure the level of circulating filarial antigenaemia (CFA). Fifty microlitres (50µl) of plasma from each sample is taken and placed in an Eppendorf microcentrifuge tube. Each sample was then diluted with 150ul of sample diluents and boiled for five minutes at 100º C in a water bath to liberate the heat stable antigen according to the manufacturer's protocol.

The samples were centrifuged at 10,000g for five minutes and 50µl of the diluted supernatant were added to the wells of the microtitre plate which had been coated with Og4C3 monoclonal antibody. Subsequently, the microtitre plates were placed in a humid chamber overnight to allow for antigen-antibody reaction. The plates were then washed with buffer provided by the manufacturer.

Fifty microlitres (50µl) of diluted rabbit anti-*Wuchereria* antibody was added to each well and incubated for one hour at room temperature. The plates were then washed again. Fifty microlitres (50µl) of anti-rabbit conjugate diluted in 600ml of antibody diluents was prepared and added to all wells and incubated for another one hour. The plates were washed and 100µl of undiluted chromogen (ABTS) was added to each well and incubated for another one hour. The plates were read with a spectrophotometer (SPECTRAmax 340, California) at 414 nm, to determine the optical density of the serum samples. Antigen units were calculated with the standard curve provided by the manufacturer (TropBio®, Australia).

Quantification of Microfilaria

The microfilaria load was estimated with Sedgewick and Giemsa counts. This involved transferring 900µl of 3% acetic acid into 1.8ml cryo tubes. The cryotubes were labelled

according to the sample. The blood samples were mixed in Monovette. One hundred microlitres (100 µl) of blood was pipetted into the cryotube containing 900 µl of 3% acetic acid and mixed thoroughly using the pipette. The solution was then poured into the Sedgewick counting chamber. Precaution was taken to ensure that there were no air bubbles in the chamber. The presence of microfilariae was observed under the microscope using X5 objective. Microfilariae within each square box were counted. The process was repeated using 975 µl of 3% acecit acid plus 25µl of blood if the mf numbers were above 500 mf/ml.

The Whartman Nucleopore® filter method involves the filtration of one ml of venous blood and passing it through a 5µm pore-size nucleopore membrane. The filters were then stained with Giemsa in a dilution of 1:20 buffer (Potassium hydrogen phosphate) for 30 minutes and the microfilariae on the filters were counted microscopically (Hoerauf *et al*., 2003; Debrah *et al.,* 2006).

Based on the microfilariae (mf) numbers from the sedgewick count, the slides were labelled indicating the study participants' ID number, amount of blood to be filtered and the date of sample collection. A 10ml syringe with the piston removed is placed onto a filter holder containing a Whatman Nucleopore® membrane filter and blood was pipetted into the syringe.

Using a second syringe 4-5 ml of water was added to the blood in the original syringe. The mixture was filtered using the piston that was removed from the first syringe into a waste container partly filled with disinfectant solution. The filter captured all the microfilariae which were present. Additional water was used to flush until all the blood was washed off. To fix the mf onto the filter in preparation for staining, 3-4 ml of methanol was flushed through the filter.

The filter was removed from the holder and placed face up on the labelled slide to dry completely. The slides were stained for 30 minutes using freshly prepared 1:20 dilution of Giemsa. The slides were then washed with water using a Pasteur pipette. The filters were then air-dried and observed under the microscope using x5 objective. The x10 objective was used to confirm the presence of mf. The mf were counted and the results recorded as mf/ ml.

Detection of Lymphedema and Staging

The study participants were examined for lymphedema. All patients being examined for lymphedema were made to stand to ensure accurate assessment. Those suffering from lymphedema were further grouped into various stages of the pathology using the Dreyer et al classification (2002) as follows;

Stage 1: These were patients who had swelling of the leg(s) but swelling was not reversible overnight. They reported that swelling increased during the day and resolved overnight when they laid prostrate in bed. To accurately classify lymphedema in stage 1, the patients were examined during late afternoon when the swelling was most visible and again in early morning to confirm that the swelling was gone.

Stage 2: Leg swelling of patients within this category was not reversible overnight. Some of the patients with stage 2 lymphedema experienced acute attacks and also had entry lesions between the toes. Some also had a mild bad odour.

Stage 3: These patients had one or more shallow skin folds which were not visible on normal legs.

Stage 4: Patients who were classified under stage 4 had bumps, lumps and protrusions termed as knobs on the skin. These knobs predisposed them to trauma and hence to further entry lesions.

None of the patients examined could be classified under stages 5, 6 or 7.

Detection of Hydrocele and Staging

The portable SonoSite 180 Plus ultrasound machine was used for ultrasound examination. The patients were examined in the supine position with legs crossed to avoid interference by movements of the patients themselves. The ultrasound gel was also kept at room temperature in order to reduce artefacts from the cremasteric muscle by a low temperature stimulus. The scrotum was then scanned in both the longitudinal and transverse sections and hydroceles were staged using the Debrah *et al.* (2007) classification;

Stage 1- Minimal fluid collection around the testis. i.e. < 0.2 cm at the upper and lower poles

Stage 2- Maximal longitudinal and transverse diameters of the hydrocele not exceeding 1.9 and 1.6 cm respectively (half screen).

Stage 3- Maximal longitudinal and transverse diameters of the hydrocele not exceeding 3.8 and 3.2 cm respectively (full screen).

Stage 4- Maximal longitudinal and transverse diameters of the hydrocele greater than 3.8 and 3.2 cm respectively.

Figure 3.1 Ultrasound Examination of Patient (Source; Original)

Statistical Analysis

Statview software and Microsoft Excel were used for data analysis. Mann-Whitney U Test was used to compare the differences in some of the study results.

CHAPTER 4 - RESULTS

Data of Study Participants

A total number of two thousand six hundred and twenty-six (2,626) people were recruited into the study after signing the informed consent forms in line with Good Clinical Practice. Their ages were recorded and each of them was interviewed to ascertain the number of rounds of ivermectin and albendazole received as at the time the study was being undertaken. Physical examinations were conducted for filarial pathologies such as lymphedema and hydrocele. Laboratory analysis of the blood samples taken from the study participants showed varying results from each village and a trend revealing the impact of the number of rounds of ivermectin and albendazole received was assessed.

Demographic Data

More men were recruited into the study than women. Out of the 2,626 study participants, 1,702 representing 64.8% were males whilst 924, representing 35.2% were females (Figure 4.1).

The ages of the study participants ranged from 18 years to 90 years and above. The age group with the highest number of study participants was 18-30 years recording 898 (34.2%) participants, followed by 31-40 years with 658 (25.1%) study participants. The number of participants decreased as the ages increased. The lowest number was 4 (0.2%) participants who were at least 91 years of age (Figure 4.2).

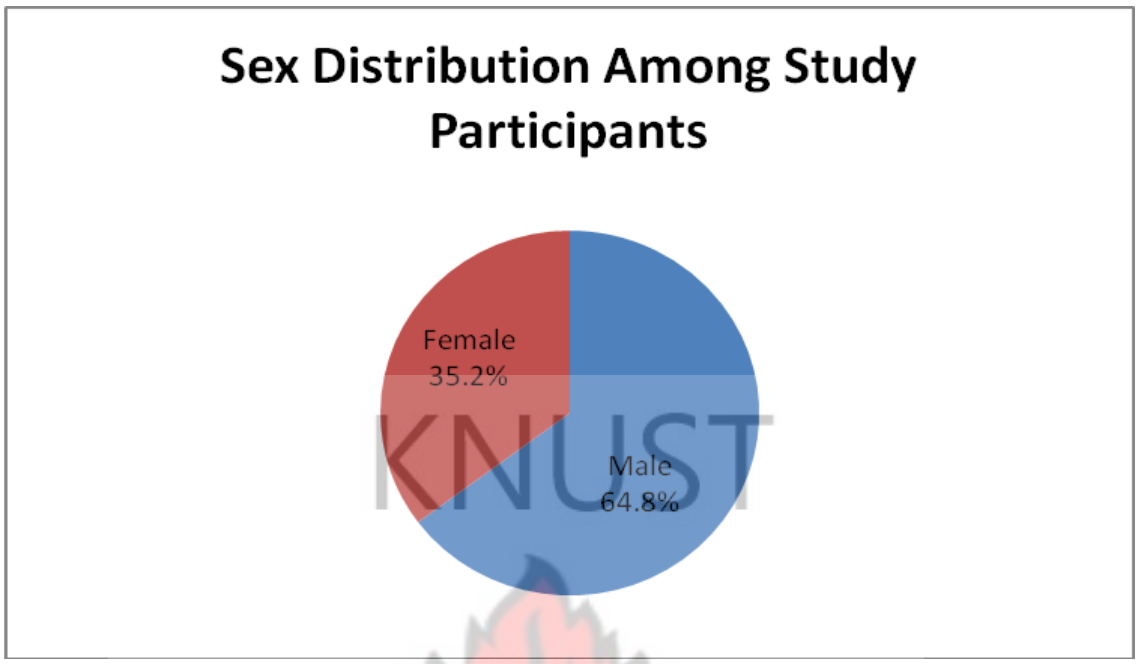


Figure 4.1 Sex Distribution Among Study Participants

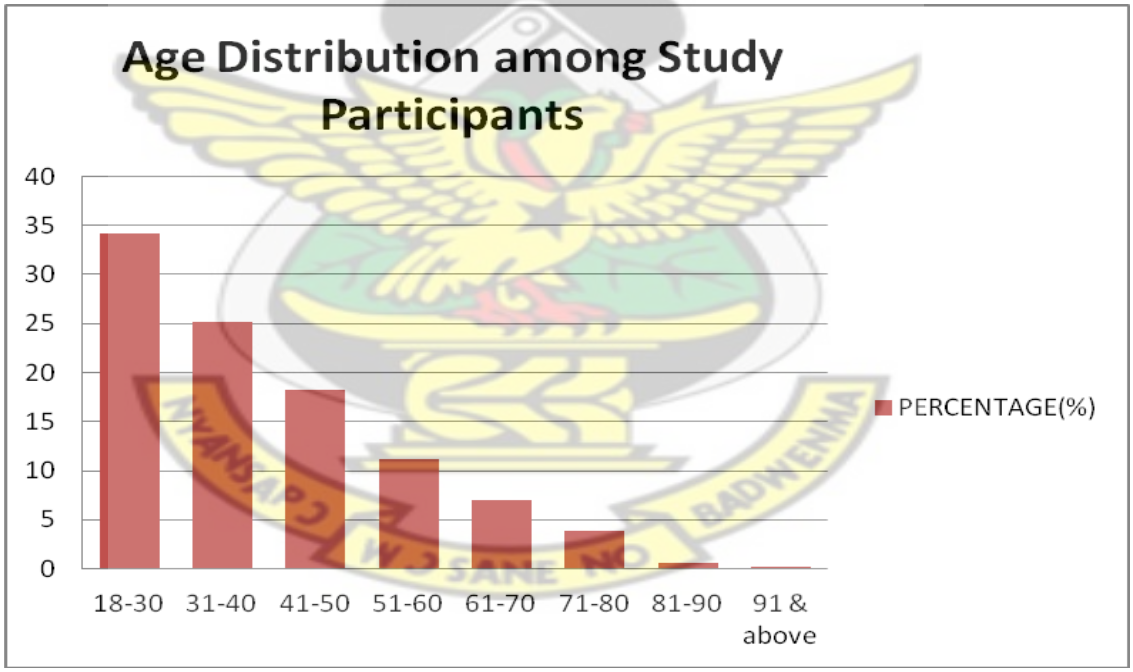


Figure 4.2 Age Distribution Among Study Participants

Prevalence of Microfilaraemia

Out of a total number of 2,626 study participants, 410 representing 15.6% tested positive for microfilaraemia. 2,216 adults, representing 84.4% tested negative for microfilaraemia (Table 4.1).

Table 4.1 Prevalence of Microfilaraemia (n=2626)

MF STATUS	FREQUENCY	PREVALENCE (%)
Positive	410	15.6
Negative	2216	84.4
TOTAL	**2626**	**100**

Prevalence of Microfilaraemia in the Study Communities

The study participants were also categorized according to the districts and villages from which they were recruited. The overall prevalence of microfilaraemia in each study district was then assessed. Out of 2496 study participants recruited from the Ahanta West District, 377 were mf-positive, resulting in prevalence of 15.1%. This was lower than in Nzema East District where 33 out of 130 people (25.4%) tested positive for microfilaraemia (Table 4.2).

Table 4.2 Prevalence of Microfilaraemia in the Study Communities

DISTRICT	NO. OF PARTICIPANTS	MF POSITIVE	PREVALENCE (%)
Ahanta West	2496	377	15.1
Nzema East	130	33	25.4
TOTAL	**2626**	**410**	**15.6**

Mann whitney U test (p value=0.0273). There was a significant difference between the two districts (Nzema-25.4%) and (Ahanta-15.1%)

Prevalence of Microfilaraemia among Males and Females

There were more males who were mf-positive than females. Out of the 410 mf-positive study participants, 356 (86.8%) were males whilst 54 of them, representing 13.2% were females (Table 4.2). For those who were mf-negative, 60.7% (1,346) were males and 39.3% (870) were females. Prevalence of microfilaraemia was 20.9% in males and 5.8% in females (i.e. 5.8%) (Table 4.3).

Table 4.3 Prevalence of Microfilaraemia among Males and Females (n=2626)

SEX	MF POSITIVE	MF NEGATIVE	PREVALENCE (%)
Male	356	1346	20.9
Female	54	870	5.8
TOTAL	**410**	**2216**	**15.6**

paired t-test (p value=0.188). No significant difference between males and females

Prevalence of Microfilaraemia among the Age Groups

Microfilaria prevalence was high (i.e. > 10%) among study participants with ages 18 to 60 years. The age group with the highest prevalence was 31-40 years, recording a prevalence of 20.5% and the lowest prevalence of 0% was recorded in those who were 91 years and above. Generally, microfilaraemia prevalence decreased with increasing ages of the study participants (Table 4.3).

Table 4.4 Prevalence of Microfilaraemia among the Age Groups (n=2626)

AGE (YRS)	NO. OF PARTICIPANTS	MF POSITIVE	MF NEGATIVE	PREVALENCE (%)
18-30	898	139	759	15.5
31-40	658	135	523	20.5
41-50	479	81	398	16.9

51-60	286	33	253	11.5
61-70	185	14	171	7.6
71-80	99	7	92	7.1
81-90	17	1	16	5.9
90 & above	4	0	4	0.0
TOTAL	**2626**	**410**	**2216**	

Prevalence of Antigenaemia

In the study conducted, the overall prevalence of antigenaemia was 39.2%. This represented 1,029 people who tested positive for the circulating filarial antigen (CFA) by the TropBio® Technique. However, 1,597 people (60.8%) were CFA negative (Table 4.6).

Table 4.5 Prevalence of Antigenaemia (n=2626)

ANTIGENAEMIA STATUS	FREQUENCY	PREVALENCE (%)
Positive	1029	39.2
Negative	1597	60.8
TOTAL	**2626**	**100**

Prevalence of Antigenaemia in the Study Communities

In this study it was revealed that prevalence of antigenaemia varied from one village to the other. The villages were grouped under Ahanta West and Nzema East districts. Antigenaemia prevalence in Nzema East was 64.6%, which was higher than in Ahanta West District where the prevalence was 37.9% (Table 4.6).

Table 4.6 Prevalence of Antigenaemia in the Study Communities

DISTRICT	NO. OF PARTICIPANTS	ANTIGENAEMIA POSITIVE	PREVALENCE (%)
Ahanta West	2496	945	37.9
Nzema East	130	84	64.6
TOTAL	**2626**	**1029**	**39.2**

Mann whitney U test (p-value=0.0256). There was a significant difference between the the two districts (Nzema-64.6%) and (Ahanta-37.9%)

Prevalence of Antigenaemia among Males and Females

Out of the 1029 study participants who were antigenaemia positive, 73.4% (755) were males whilst 26.6% (274) were females (Table 4.7). Out of the 1,597 CFA-negative participants, 947, representing 59.3%, were males and 650, representing 40.7%, were females. Prevalence of antigenaemia among males was therefore 44.4% and that of females was 29.7%.

Table 4.7 Prevalence of Antigenaemia among Males and Females (n=2626)

SEX	ANTIGENAEMIA POSITIVE	ANTIGENAEMIA NEGATIVE	PREVALENCE (%)
Male	755	947	44.4
Female	274	650	29.7
TOTAL	**1029**	**1597**	**39.2**

Paired T-test (p value = 0.191). No significant difference between males and females

Prevalence of Antigenaemia among the Age Groups

From the data analysis conducted, the age group with the highest prevalence of antigenaemia was 90 years and above recording a prevalence of 50%. The prevalence rate peaked at 42.9% for age group 31- 40 years and then generally declined as the ages increased (Table 4.8).

Table 4.8 Prevalence of Antigenaemia among the Age Groups (n=2626)

Age (yrs)	No. Of Participants	Antigenaemia Positive	Antigenaemia Negative	Prevalence (%)
18-30	898	358	540	39.9
31-40	651	279	372	42.9
41-50	479	186	293	38.8
51-60	293	80	213	27.3
61-70	185	64	121	34.6
71-80	99	27	72	27.3
81-90	17	6	11	35.3
91 & above	4	2	2	50.0
TOTAL	**2626**	**1002**	**1624**	

Variation of Age with Microfilaraemia and Antigenaemia Prevalence

Generally, antigenaemia prevalence in the various age groups was higher than microfilaraemia prevalence. The prevalence rates peaked at 31-40 years age group for both curves and generally declined as the ages increased. The antigenaemia prevalence for those 91 years and above can be considered an outlier since only 4 participants were recruited, 2 of whom tested positive for antigenaemia. This is what accounted for the high prevalence of 50% recorded for that age group (Figure 4.3).

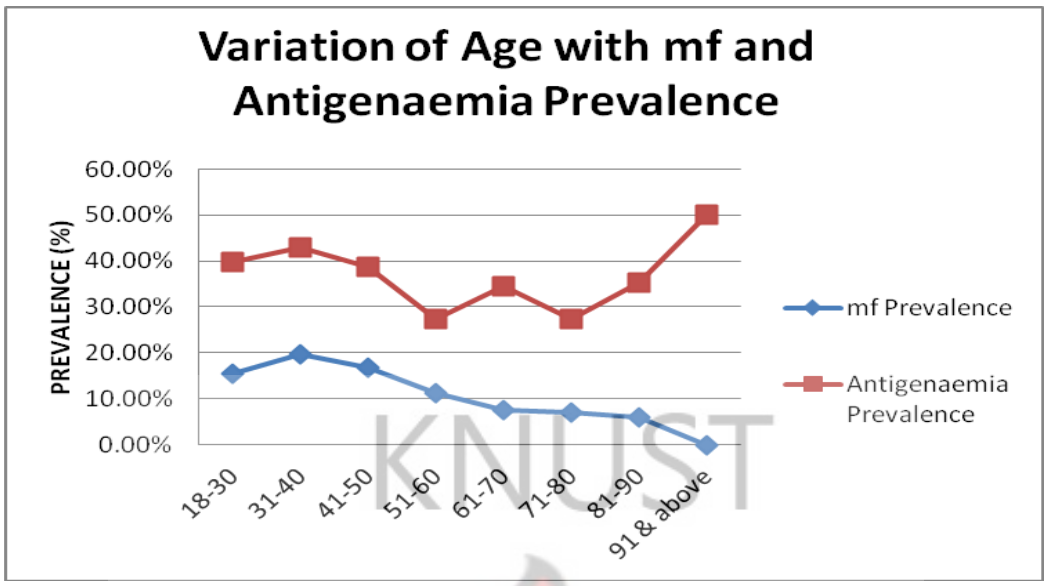


Figure 4.3 Variation of Age with Antigenaemia and mf Prevalence

Prevalence of Hydrocele

The total number of males recruited into the study was 1702. Out of this, 686 were found to be suffering from hydrocele. This gave an overall prevalence of 40.3%

Table 4.9 Prevalence of Hydrocele (n=1702)

HYDROCELE STATUS	FREQUENCY	PREVALENCE (%)
Positive	686	40.3
Negative	1016	59.7
TOTAL	**1702**	**100**

Prevalence of Hydrocele in Study Communities

The prevalence of hydrocele among the study communities varied from one village to the other and from one district to the other. The prevalence recorded in the Ahanta West district was 26.4% greater than that recorded in the Nzema East district which was 20.8% (Table 4.10).

Table 4.10 Prevalence of Hydrocele in the Study Communities

DISTRICT	NO. OF PARTICIPANTS	HYDROCELE POSITIVE	PREVALENCE (%)
Ahanta West	2496	659	26.4
Nzema East	130	27	20.8
TOTAL	**2626**	**686**	**26.1**

Mann whitney u test (p value=0.003) Significant difference between the two districts

Prevalence of Hydrocele among Age Groups

The age group that recorded the highest prevalence was 18-30 years, with prevalence rate of 29.9%. This was followed by those within the 31-40 years age group recording a prevalence rate of 28%. The prevalence rates subsequently declined as the ages increased till a prevalence of 0.7%, recorded for those 81-90 years of age (Table 4.11).

Table 4.11 Prevalence of Hydrocele among Age Groups (n=686)

AGE (YRS)	HYDROCELE POSITIVE	PREVALENCE
18-30	205	29.9%
31-40	192	28.0%
41-50	122	17.8%
51-60	75	10.9%
61-70	54	7.9%
71-80	33	4.8%
81-90	5	0.7%
TOTAL	**686**	**100%**

Prevalence of the Various Stages of Hydrocele

Using the Debrah *et al* (2011) classification, patients with hydrocele were grouped into the various stages of hydrocele. Prevalence of stage 1 was approximately 52% (52.2%). This was the highest, followed by stage 4 which recorded a prevalence of 20%. Prevalence rates for stage 2 and stage 3 were 18% and 11% respectively (Figure 4.4).

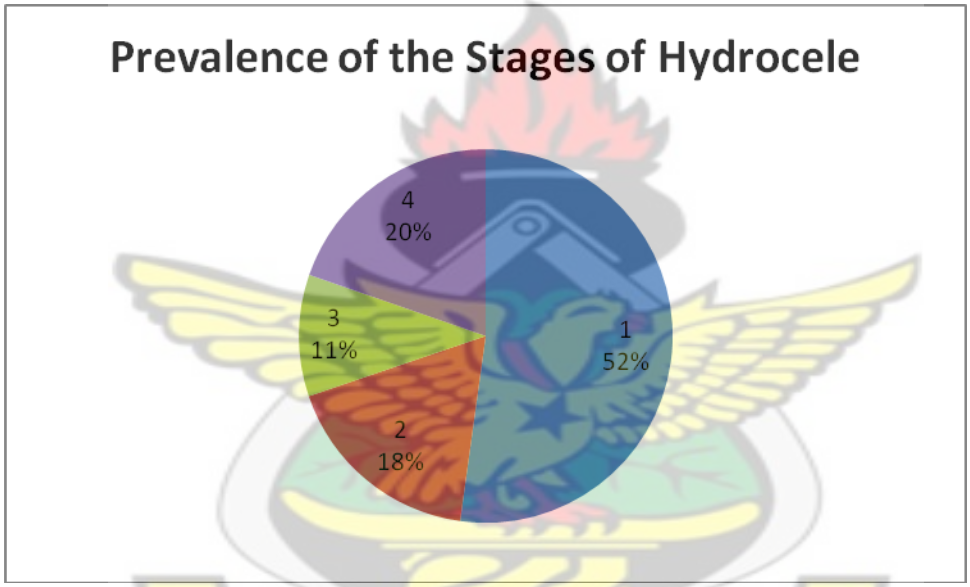


Figure 4.4 Prevalence of the various stages of hydrocele

Prevalence of Lymphedema

Out of the 2626 participants recruited into the study, 266 had lymphedema and the remaining 2359 representing 89.8% had no lymphedema. This resulted in a lymphedema prevalence of 10.2% (Table 4.12).

Table 4.12 Prevalence of Lymphedema (n=2626)

LYMPHEDEMA STATUS	FREQUENCY	PREVALENCE (%)
Positive	266	10.1
Negative	2359	89.8
TOTAL	**2626**	**100**

Prevalence of Lymphedema among Males and Females

The number of females suffering from lymphedema was 188 representing 70.8%, whilst 78 males, representing 29.2% had lymphedema (Table 4.13).

Table 4.13 Prevalence of Lymphedema among Males and Females (n=266)

SEX	LYMPHEDEMA POSITIVE	PREVALENCE (%)
Male	78	29.3
Female	188	70.7
TOTAL	**267**	**100.0**

Paired T-test (p value = 0.271). No significant difference between males and females

Prevalence of Lymphedema among Age Groups

Lymphedema prevalence was highest in the age group 18-30 years, recording a prevalence rate of 39.1%. Those within 31-40 years recorded a prevalence of 30.1%. The prevalence rate

decreased as the ages increased till the age group 81-90 years which recorded a prevalence of 0.4% (Table 4.14).

Table 4.14 Prevalence of Lymphedema among Age Groups (n=266)

AGE (YRS)	LYMPHEDEMA POSITIVE	PREVALENCE
18-30	104	39.1%
31-40	80	30.1%
41-50	44	16.5%
51-60	22	8.3%
61-70	10	3.8%
71-80	5	1.9%
81-90	1	0.4%
TOTAL	**266**	**100%**

Prevalence of the Various Stages of Lymphedema

Using the Dreyer et al classification (2002), the prevalence of lymphedema for each of the stages of lymphedema was assessed. Lymphedema stage 2 recorded the hihest prevalence of 50% followed by stage 1 with a prevalence rate of 38%. Prevalence rates of stage 3 and stage 4 were 7% and 5% respectively (Figure 4.5).

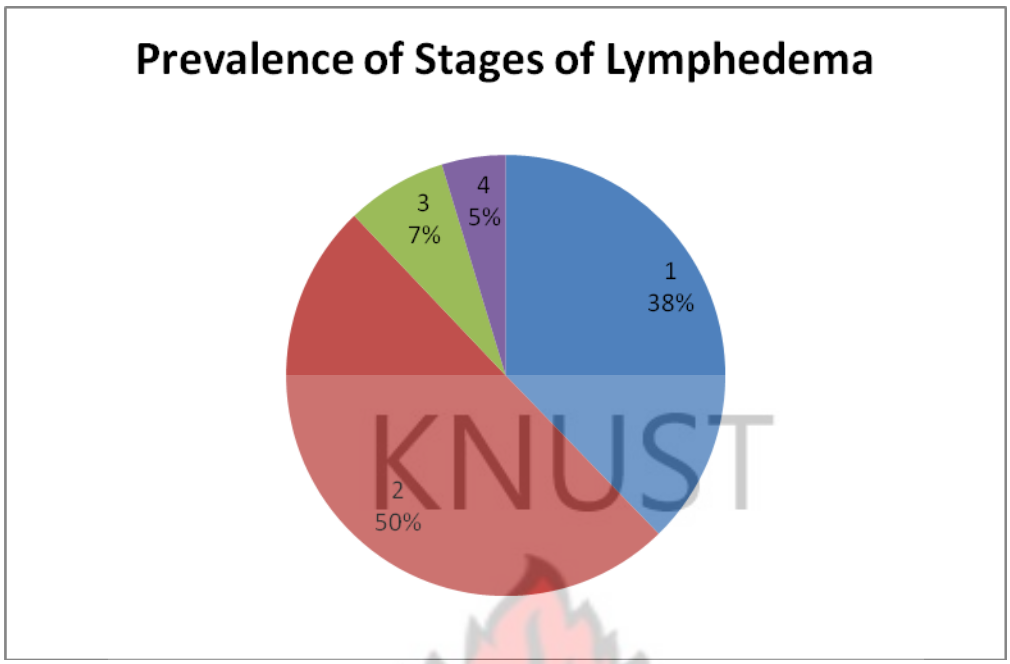


Figure 4.5 Prevalence of the Various Stages of Lymphedema

Compliance to IVM+Albendazole by the Study Participants

Six hundred and thirty-two (632), representing 24.1% of the study participants had never received any ivermectin-albendazole treatment; 11.4 % had received treatment once and 21.7% had taken 3 rounds of treatment. The study revealed that only 2.4% of the study participants had completed 6 rounds of treatment. As the number of rounds of treatment increased, the lower the number of participants recorded, showing a high level of non-compliance (Table 4.15).

Table 4.15 Compliance to IVM+Albendazole by Study Participants

IVM ROUNDS	NO. OF PARTICIPANTS	PERCENTAGE(%)
0	632	24.1
1	300	11.4
2	447	17.0
3	569	21.7

4	383	14.6
5	183	7.0
6	64	2.4
7	18	0.7
8	7	0.3
9	8	0.3
10	5	0.2
11	2	0.1
13	7	0.3
15	1	0.0
TOTAL	**2626**	**100%**

Compliance to IVM+Albendazole Rounds by the Age Groups

An analysis of the number of rounds of ivermectin and albendazole combination received by the study population revealed that compliance to the annual mass drug administration differed from one age group to the other. A total number of 632 people had never received any treatment. Out of this, 258 people representing 40.8% were within the 18-30 years age group. As the number of rounds increased, the number of study participants decreased. The number of study participants who had never received any rounds of treatment also decreased as the ages increased.

Comparing this trend with those who had received six (6) rounds of treatment, which is the minimum recommended by the WHO, only 10 people (approximately 15.6%) belonging to the 18-30 year group had complied with treatment. The highest number of people who had received 6 rounds of ivermectin and albendazole were 41-50 years who recorded 26.6%.

Compliance, therefore, was lower in the younger age group than the older ones.

Table 4.16 IVM+Albendazole Rounds According to the Various Age Groups (n=2626)

	IVM ROUNDS													
AGE (yrs)	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**13**	**15**
18-30	258(40.8%)	135	165	183	80	57	10(15.6%)	5	2	1	0	0	2	1

31-40	152 (24.1%)	83	108	134	109	40	14(21.9%)	2	3	1	1	2	2	0
41-50	103(16.3%)	36	87	101	89	39	17(26.6%)	2	1	2	1	0	1	0
51-60	42(6.6%)	27	41	78	46	31	13(20.3%)	5	1	4	3	0	2	0
61-70	47(7.4%)	11	28	68	35	12	7(10.9%)	3	0	0	0	0	0	0
71-80	24(3.8%)	8	14	0	20	4	3(4.7%)	0	0	0	0	0	0	0
81-90	4(0.6%)	0	2	5	4	0	1(1.6%)	1	0	0	0	0	0	0
91 & above	2(0.3%)	0	2	0	0	0	0(0%)	0	0	0	0	0	0	0
TOTAL	**632**	**300**	**447**	**569**	**383**	**183**	**64**	**18**	**7**	**8**	**5**	**2**	**7**	**1**

Compliance to IVM+Albendazole Rounds by the Males and Females

It was observed that within the study population, more males than females had never participated in the annual mass drug administration. Out of a total of 632 people who had never received the combined ivermectin-albendazole treatment, 504 (i.e. 79.7%) were males whilst the remaining 128 (i.e. 20.3%) were females.

As the rounds of treatment increased, the proportion of males decreased whilst that of females who had complied with the treatment increased. The percentages were almost 50% each for those who had received 5 rounds of treatment. Out of 183 study participants, 92 of them representing 50.3% were males whilst 91 (i.e. 49.7%) were females. Similar results were obtained for those who had received 6 rounds of treatment, which is the minimum recommended by the WHO.

There was therefore a higher non-compliance to treatment among males than females.

Table 4.17 IVM+Albendazole Rounds According to Males and Females (n=2626)

	IVM ROUNDS													
SEX	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**13**	**15**
Male	504(79.7%)	220	280	306	223	92	38(58.5%)	10	6	6	5	2	7	1
Female	128 (20.3%)	80	164	263	160	91	27(41.5%)	8	1	4	0	0	0	0
TOTAL	**632**	**300**	**444**	**569**	**383**	**183**	**65**	**18**	**7**	**10**	**5**	**2**	**7**	**1**

Relationship between Rounds of IVM+Albendazole and Microfilaraemia

Out of 410 study participants who tested positive for microfilaraemia, 119 representing 29% had never received IVM+albendazole treatment. This was the highest prevalence of microfilaraemia followed by those who had received 3 rounds of treatment whose prevalence rate was 18.8%.

Approximately 99% of those who tested positive for microfilaraemia had received less than 6 rounds of treatment which is the minimum recommended by the WHO. This showed a high non-compliance rate among the study population. Generally, the prevalence decreased as the number of rounds of ivermectin received increased.

Microfilaraemia prevalence among those who had received 6 rounds of IVM+albendazole treatment was 1.2%. The prevalence rate, however, remained less than 1% among those who had received at least 7 rounds of treatment (Table 4.18).

Table 4.18 Relationship between Rounds of IVM+Albendazole and MF Prevalence (n=410)

IVM ROUNDS	MF POSITIVE	PREVALENCE (%)
0	119	29.0
1	61	14.9
2	71	17.3
3	77	18.8
4	55	13.4

5	21	5.1
6	5	1.2
7	0	0.0
8	0	0.0
9	0	0.0
10	1	0.2
TOTAL	**410**	**100**

Relationship between Rounds of IVM+Albendazole and Antigenaemia Prevalence

The highest number of people who tested positive for the circulating filarial antigen was 228 with a prevalence rate of 22.8%. This represented those who had never received any ivermectin treatment. The lowest prevalence of antigenaemia recorded was 0.1%. This represented those who had received 10 rounds of ivermectin plus albendazole treatment as part of the Mass Drug Administration (MDA). Between those who had only 1 round of treatment and those who received 3 rounds of treatment, there was a gradual increase in antigenaemia prevalence but generally, as the number of rounds of treatment increased, prevalence rate decreased.

Antigenaemia prevalence was less than 1% among study participants who had received more than 6 rounds of treatment (Table 4.19).

Table 4.19 Relationship between Rounds of IVM+Albendazole and Antigenaemia Prevalence (n=1002)

IVM ROUNDS	ANTIGENAEMIA POSITIVE	PREVALENCE (%)
0	228	22.8
1	132	13.2
2	190	19.0
3	206	20.6
4	149	14.9
5	65	6.5
6	21	2.1
7	6	0.6
8	2	0.2
9	2	0.2
10	1	0.1
TOTAL	**1002**	**100**

Relationship between IVM+Albendazole Rounds and Hydrocele Prevalence

The data from the study revealed that prevalence of hydrocele was generally high in participants with lower number of rounds of ivermectin and albendazole treatment. The highest prevalence of 21.7% was recorded among those who had never participated in the

annual mass drug administration. As the number of rounds increased, the prevalence rate decreased. Those who had received at least 7 rounds of IVM+Albendazole treatment recorded prevalence rates less than 1% (Table 4.20).

Table 4.20 Relationship between IVM+Albendazole Rounds and Hydrocele Prevalence

IVM ROUNDS	HYDROCELE POSITIVE	PREVALENCE (%)
0	149	21.7
1	89	13.0
2	137	20.0
3	136	19.8
4	107	15.6
5	40	5.8
6	20	2.9
7	3	0.4
9	3	0.4
10	2	0.3
TOTAL	**686**	**100**

Relationship between Rounds of ivermectin and Prevalence of Lymphedema

Two hundred and sixty-six (266) study participants suffered from lymphedema. Out of this, 77 of them, representing 28.9% had not received any ivermectin plus albendazole treatment before. Those who had received a minimum of seven (7) rounds of ivermectin, on the average, recorded very low prevalence (<1.0%) of lymphedema. It was therefore observed that the higher the number of rounds of treatment received, the lower the prevalence of lymphedema (Table 4.21).

Table 4.21 Relationship between Rounds of IVM+Albendazole and Lymphedema Prevalence(n=266)

IVM ROUNDS	LYMPHEDEMA POSITIVE	PREVALENCE(%)
0	77	28.9
1	28	10.5
2	44	16.5
3	52	19.5
4	39	14.7
5	15	5.6
6	5	1.9
7	1	0.4
8	1	0.4
9	1	0.4
10	1	0.4
11	0	0.0
13	2	0.8
15	0	0.0
TOTAL	**266**	**100**

CHAPTER 5- DISCUSSIONS

Lymphatic filariasis is a disease of grave public health concern and continues to pose an increasing socioeconomic and psychosocial burden on the infected individuals and the communities in which they live (WHO, 2002). In spite of the problems the disease poses, it is still classified as a neglected tropical disease. Since the implementation of the Mass Drug Administration (MDA) in the year 2000, there is little data on its impact on the prevalence of lymphatic filariasis.

A study conducted in the Ahanta West District in 1995 showed that by employing methods like interviews, group discussions, questionnaires and physical examinations, it was possible to obtain estimates of lymphatic filariasis burden in a community (Gyapong *et al.*, 2009).

This cross-sectional study therefore sought to determine the prevalence of lymphatic filariasis and its pathologies in the Nzema East and Ahanta West districts. The study also sought to assess the impact of the annual mass drug administration (MDA) programme on infection prevalence and to make recommendations on how this very important programme can be further enhanced.

Globally, the impact of the GPELF and the MDA has been enormous. Recent data indicate that since the beginning of the MDA, lymphatic filariasis transmission among at-risk populations has dropped by 43% (Ottesen *et al.,* 2011). In Ghana, the prevalence rate of microfilaraemia was estimated to be between 11% and 41% and that of antigenaemia was between 30% and 49% (WHO, 2002).

In this study, a total of 2626 people living in the Ahanta West and Nzema East Districts were examined. The overall prevalence of microfilaraemia and antigenaemia were 15.6% and 39.2% respectively. These figures are high since the target by the World Health Organization for lymphatic filariasis not to be considered a public health problem is a prevalence rate below 1%. The poor expected outcome of MDA in endemic regions where multiple rounds have been performed may be attributed to the fact that ivermectin and albendazole combination is considered inferior to diethylcarbamazine and albendazole due to their high macrofilaricidal activities (Awadzi *et al.*, 2004; Osei Atweneboana *et al*., 2007).

It is however worth-noting that the prevalence rates of microfilaraemia and antigenaemia were extremely low in study populations that had received at least 6 rounds of ivermectin and albendazole as part of the annual mass drug administration.

Out of 410 people who were microfilaraemia positive (mf+), only five (5) had received six (6) rounds of ivermectin and albendazole. This represented a prevalence rate of 1.2%. Prevalence rate among those who had received seven (7) rounds or more of treatment was consistently less than 1%.

The results for antigenaemia prevalence were similar to those for microfilaraemia prevalence. Out of a total of 1,002 study participants who tested positive for circulating filarial antigen, 21 of them, representing 1.2% had received six (6) rounds of ivermectin and albendazole. For those who had received at least seven (7) rounds of treatment, the prevalence remained less than 1%.

It is postulated that the number of rounds of ivermectin required to reduce the prevalence of microfilaraemia to less than 1% depends on the following factors;

- Baseline prevalence of microfilaraemia
- The population's compliance with MDA. Treatment coverage should be at least 65%
- The presence of an effective programme for vector control

In areas with intense transmission and less compliance, a longer duration of MDA may be required (GPELF Progress Report, 2005).

It was observed from this study that even though MDA has been implemented in the study area for more than ten years, a significant majority (97%) of the study participants had received less than 6 rounds of ivermectin and albendazole treatment. This shows that there is a low compliance rate among the inhabitants of the Ahanta West and Nzema East districts.

In another study conducted on treatment compliance in the Ahanta West District, 20% of the treated population complied with five (5) consecutive rounds of treatment and less than 5% had not received any ivermectin treatment at all. A significant 75% of the study participants took 2-4 rounds of treatment during a 5-year period (WHO, 2006).

Maged *et al* reported an overall compliance rate of 86.7%, 95.5%, 90.1% and 88.8% for MDA rounds between 1 and 4. This has resulted in a low prevalence of microfilaraemia and antigenaemia in study populations (Maged *et al.*, 2007).

A number of factors may account for the apparent unwillingness of the people to participate in the annual free distribution of ivermectin and albendazole. Whilst some of them do not start the MDA programme at all, majority of them take the first dose but are not consistent in participating in the MDA in the subsequent years. The main reason accounting for this is the fear of experiencing adverse reactions sometimes associated with the drugs. Some of these may include urticaria, itching, low grade fever and chills and swelling of the face and limbs.

Adverse effects of ivermectin usually corresponds with the microfilarial load; the higher the microfilaraemia, the higher the incidence of adverse reactions (Taylor *et al.*, 2010). Adverse events, especially signs of encephalopathy, are also common in areas with co-endemicity for loiasis (Wanji *et al.*, 2009).

The adverse reactions associated with diethylcarbamazine and ivermectin are also thought to be caused by the rapid release of microfilariae material and *Wolbachia* endosymbiont bacteria into the blood (Cross *et al.*, 2001; Molyneux *et al.*, 2003).

Doxycycline has been found to be safe and effective in the treatment of lymphatic filariasis. Four (4) to eight (8) week course of 200mg/day lead to a gradual and sustained loss of microfilariae from host blood (Debrah *et al*., 2007; 2009; Hoerauf *et al.*, 2003; Taylor *et al.*, 2005). Doxycycline also has anti-wolbachia properties hence by administering a 3-week course of doxycline with ivermectin and albendazole, there can be a significant reduction in microfilariaemia (Debrah *et al.*, 2007; 2009; Turner *et al.*, 2006). This can mitigate the adverse reactions experienced after taking the standard treatment and hence enhance compliance among endemic populations.

Secondly, the low compliance can be attributed to the fact that some of the inhabitants in endemic communities continue to doubt that lymphatic filariasis, characterised by swollen limbs and fluid accumulation, is caused by a worm and transmitted by a mosquito. Due to the high illiteracy rates in those communities, some of the people continue to assign superstition and spirituality as the cause of the filarial pathologies. It is therefore difficult to convince such people to participate in the annual intake of ivermectin and albendazole as a means of curbing the menace.

A study conducted in Nigeria in 2010 showed that only 36.1% of the population accepts the fact that lymphatic filariasis is caused by mosquito bites. Comparing knowledge levels between males and females, 43.9% of female respondents attributed the cause of disease to walking long distance and stepping on charms. Among males, 41.9% of respondents identified good hygiene and avoidance of mosquito bite as ways of preventing infection. These differences, with $p<0.05$, were found to be statistically significant (Omudu *et al.*, 2011).

Furthermore, lymphatic filariasis continues to suffer from a lack of the necessary commitment and attention from policy makers and health promotion leaders in the communities in which the disease is endemic. An evidence of this is the lack or absence of effective and intensive public education campaigns on the disease. The at-risk population and those already infected are therefore not well informed about the benefits of the annual mass drug administration and the need for them to participate.

Not only do the MDA drugs prevent the spread of lymphatic filariasis, they also stop the progression of disease in those already infected (WHO, GPELF Report, 2000-2009).

Results from this study on the relationship between rounds of IVM+albendazole received and the prevalence of lymphedema and hydrocele pathologies showed that as the number of rounds of treatment increased among the study population, the prevalence of lymphedema and hydrocele pathologies decreased.

Prevalence of lymphedema among those who had never received ivermectin plus albendazole treatment was 28.9%. For those who had received only 3 rounds of treatment, lymphedema prevalence was 19.6%. The rate however remained less than 1% among those who had received more than six (6) rounds of treatment.

Similar results were recorded for hydrocele prevalence. The highest prevalence of 21.7% was recorded for study participants who had never received any treatment and the lowest prevalence was 0.3% which was recorded among those who had received 10 rounds of IVM+Albendazole treatment.

In a cross-sectional study conducted in Thiruvananthapuram district of Kerala, India (Nujum *et al.,* 2012), a comparison was done between compliant and noncompliant individuals. The independent factors determining noncompliance were client attitude of not perceiving the need, an unfavorable provider attitude and low drug administrator acceptability.

The study showed that health workers or community volunteers were the most common source of knowledge regarding MDA (48.5%), followed by Television (20.7%) and newspapers (10.1%). Low acceptability of drug administrator, low acceptability of drug and unfavourable provider attitude were factors determining noncompliance (Nujum *et al.*, 2012).

Even though the MDA programme has been implemented in the Ahanta West and Nzema East districts for more than ten years, it was revealed from the study that approximately 97% of the study participants had received less than 6 rounds of treatment. This high non-compliance rate explains the high prevalence of infection and pathologies recorded.

Results from the study showed a poor compliance to treatment by males as compared to females. It was observed that out of the 632 study participants who had never received any treatment, 79.7% of them were males whilst 20.3% were females. Microfilaraemia and antigenaemia prevalence rates were correspondingly higher in males than in females. Prevalence of microfilaraemia among males was 20.9% and 5.8% among females. For those who were antigenaemia positive, 44.4% were males and 29.7% were females.

A study in 1990 involving 53 countries from Africa, South East Asia, the Indian Subcontinent and the Americas showed a lower mean prevalence of infection in females than in males. Prevalence was consistently lower in women of reproductive age. Density of infection was also lower in the reproductive age but higher in children and in older women. Clinical disease was also found to be lower in women and pathologies, such as lymphedema, had a later age of onset and rise to peak prevalence than in males (Brabin, 1990).

It was suggested that females had less exposure to infective vectors than males. Males, who are mainly farmers and fishermen, spend longer hours outside the home and hence

are exposed to bites by infected mosquitoes as compared to women whose activities are commonly domestic.

Several investigators have also suggested that females have increased resistance to infection. This is supported by serological studies showing high antibody positivity to adult worm antigens in females (Brabin, 1990).

Data from this study also showed a high non-compliance rate among younger age groups; as the ages of the study participants increased, compliance to treatment increased. The age group with the highest non-compliance was 18-30 years. This age group comprised 40.8% of the total number of participants who had never received ivermectin and albendazole treatment. This was reflected in a high prevalence of 39.9% and 15.5%, respectively, in antigenaemia and microfilaraemia. This was the second highest prevalence recorded among the age groups after age 31- 40 years. The prevalence rates of lymphedema and hydrocele, i.e. 39.1% and 29.9%, were however the highest recorded among all the age groups.

It is unclear what may account for the high non-compliance among the young age group except to suggest that the youth characteristically always pose a challenge to health project implementers. They very often require more education and some form of motivation to encourage them to comply with disease prevention programmes.

Secondly, people attribute the use of drugs only to treatment and not for prophylaxis. Young people often attribute the occurrence of chronic diseases to old age. Health education should therefore focus on the debilitating effect of the disease and the need for prevention through compliance with the annual drug administration.

CHAPTER 6- CONCLUSION

Globally, the World Health Organization (WHO) through the Global Programme to Eliminate Lymphatic Filariasis (GPELF) has made immense efforts at reducing the transmission of lymphatic filariaisis and minimise the morbidities associated with it. After more than ten (10) years of implementing the Mass Drug Administration (MDA), Ghana appears to be far behind in meeting the WHO target of <1% prevalence. Prevalence rates for microfilaraemia (16.9%), antigenaemia (44.4%), lymphedema (35.2%) and Hydrocele (40.3%) recorded in this study emphasise the need for more work to be done. The trend observed in which the prevalence rates declined as the number of rounds of ivermectin received increased also supports the fact that there is a high non-compliance to the annual mass drug administration programme. These, and the lack of an effective and more aggressive strategy to control the mosquito vector, make it almost impossible for Ghana to eliminate lymphatic filariasis by 2020.

RECOMMENDATIONS

1. The mass drug administration has proven to be an effective way of controlling lymphatic filariasis. It should therefore be sustained and promoted globally.

2. The number of rounds of ivermectin and albendazole recommended by the WHO to achieve <1% microfilaraemia should be increased from 6 to at least 7 rounds.

3. An intensive education campaign on lymphatic filariasis should be organised nationwide with emphasis on endemic areas. The education should focus on the

need for compliance, protection of individuals from mosquito bites and dispel superstitious beliefs as a cause of infection.

4. People living in endemic areas, especially the youth, should be encouraged to participate annually in the mass drug administration and should achieve a minimum of 7 rounds of treatment.

5. In MDA, the person giving the drug to the beneficiary is the most important person, whose attitude and acceptability determines compliance. More rigorous selection and training of drug administrators are essential to enhance the compliance level.

6. Encourage early detection and treatment of filarial pathologies (eg. Lymphedema) to minimize pain and disability.

7. There is the need to institute an effective vector control programme as a means of interrupting disease transmission

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